COGNITIVE FUNCTIONING AND NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR), AND MONOCYTE LYMPHOCYTE RATIO (MLR) IN BIPOLAR AFFECTIVE DISORDER

A THESIS SUBMITTED TO

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT (PUNJAB)

IN THE PARTIAL FULFILLMENT

FOR THE AWARD OF DEGREE OF

DOCTOR OF MEDICINE

IN

PSYCHIATRY

2024

Submitted By

DR SANDEEP KAUR DHILLON

DEPARTMENT OF PSYCHIATRY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA, PUNJAB

DECLARATION BY THE CANDIDATE

I hereby declare that the thesis entitled "**COGNITIVE FUNCTIONING AND NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR) AND MONOCYTE LYMPHOCYTE RATIO (MLR) IN BIPOLAR AFFECTIVE DISORDER"** submitted towards partial fulfillment of the requirements for the award of **MD in Psychiatry** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Navkiran S. Mahajan** Professor & Head Department of Psychiatry, **Dr. Ranjive Mahajan,** Former Professor & Head, Department of Psychiatry, **and Dr. Bhavna Malhotra,** Professor, Department of Pathology. No part of this thesis has formed the basis for the award of any degree previously.

_____

Dr. SANDEEP KAUR DHILLON
Department of Psychiatry,
Dayanand Medical College & Hospital,
Ludhiana, Punjab

Date:

Place:

CERTIFICATE OF SUPERVISORS

This is to certify that the work incorporated in this thesis entitled"**COGNITIVE FUNCTIONING AND NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR) AND MONOCYTE LYMPHOCYTE RATIO (MLR) IN BIPOLAR AFFECTIVE DISORDER"**has been carried out by **Dr. Sandeep Kaur Dhillon** under our direct supervision. The data incorporated in this thesis is original and genuine and has been carried out by the candidate herself.

Signature of Supervisor **Signature of Co-Supervisors**

Dr. Navkiran S. Mahajan
Professor& Head
Department of Psychiatry
DMC&H, Ludhiana

Dr. Ranjive Mahajan
Former Professor & Head
Department ofPsychiatry,
DMC&H, Ludhiana

Dr. Bhavna Malhotra
Professor
Department of Pathology
DMC&H, Ludhiana

Date:

ENDORSEMENT BY THE HEAD OF THE INSTITUTE

This is to certify that the thesis entitled **"COGNITIVE FUNCTIONING AND NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR) AND MONOCYTE LYMPHOCYTE RATIO (MLR) IN BIPOLAR AFFECTIVE DISORDER"**is a bonafide research work done by **Dr.Sandeep Kaur Dhillon** under the supervision of **Dr. Navkiran S. Mahajan,** Professor& Head, Department of Psychiatry, **Dr. Ranjive Mahajan,** Former Professor & Head, Department of Psychiatry **and Dr. Bhavna Malhotra,** Professor, Department of Pathology.

Principal

Dr. Gurpreet Singh Wander
Principal
DMC&H, Ludhiana

Date:

COPYRIGHT

Declaration by the Candidate

I hereby declare that the Baba Farid University of Health Sciences, Faridkot, shall have the right to preserve & use this thesis in print or electronic format for academic/study purposes by the research scholar/students.

Signature

Dr. Sandeep Kaur Dhillon
Department of Psychiatry,
Dayanand Medical College & Hospital,
Ludhiana, Punjab - 141001

Date:

© Baba Farid University of Health Sciences, Faridkot

Dedicated to

my parents,

teachers, and

friends

ACKNOWLEDGEMENT

"Create the highest, grandest vision possible for your life, because you become what you believe." ~ Oprah Winfrey

I express my deepest gratitude to the Divine for providing me with the strength, wisdom, resilience, and perseverance necessary to embark on and complete this project. Without these blessings, this achievement would not have been possible.

Throughout my academic pursuit of this degree, Dr. Navkiran S. Mahajan, Professor and Head, Department of Psychiatry at Dayanand Medical College and Hospital, Ludhiana, has been a mentor, source of inspiration, and role model. She allowed me the freedom to explore my research interests while quietly guiding me to stay focused on the essence of my study. Her expert guidance was instrumental in the completion of this thesis, and I will always value her invaluable mentorship.

I am profoundly grateful to my co-guide, Dr. Ranjive Mahajan, Former Professor and Head, Department of Psychiatry at Dayanand Medical College and Hospital Ludhiana, for his exceptional guidance, encouragement and unwavering support throughout this thesis. His expert advice and thoughtful feedback were crucial to achieving the project's goals. Additionally, I extend my thanks to Dr. Bhavna Malhotra, Professor, Department of Pathology, for her steadfast guidance and support during the project. I also wish to thank Dr. Pankaj Kumar, Professor,

Department of Psychiatry, and Dr. Mitthat Miglani, Assistant Professor, Department of Psychiatry, for their kind assistance, invaluable guidance, and unwavering support.

I am deeply thankful to my grandparents, my father, Mr. Raj Bahadur Singh Dhillon, my mother, Mrs. Gurmeet Kaur Dhillon, my brother, Ajaydeep Singh Dhillon, and my sisters, Alish Gill and Amrit Sarai, for their moral backing, constant support, and encouragement, which have enabled me to accomplish this endeavor.

Additionally, I extend my thanks to my senior residents, Dr. Mantaz Dhillon, Dr. Gabby Sethi, and Dr. Cherry Sikka, as well as my seniors, Dr. Aarti Gupta and Dr. Ardaaspreet Singh Sandhu. I also thank numerous other individuals, including my batch mates, Dr. Alisha Aluna and Dr. Nitin Baldeep Singh Duggal, and my juniors, Dr. Rakshanda Vashisht, Dr. Shagufta Ali, Dr. Kimi Garg, Dr. Robin Singla, Dr. Harmanjot Singh, and Dr. Prince Jindal, along with my other teachers, family, well-wishers, and colleagues, for their timely assistance and support in completing this study. I would also like to thank my friends Dr. Ravipartap Singh Grewal, Dr. Priyanka Seth, Dr. Akram Brar, Dr. Divjot Kaur, Dr. Sagal Pannu, and Niharika, for their constant encouragement and inspiration during my challenging times.

At the end of my thesis, I would like to express my deep appreciation to everyone who made this project achievable and memorable. I am particularly thankful to the patients for their cooperation and to the technical staff for their dedicated assistance. Their collective support has been invaluable, helping me navigate challenges and ensuring the successful completion of my work.

Dr. Sandeep Kaur Dhillon

LIST OF ABBREVIATIONS

BAC- A	BRIEF ASSESSMENT OF COGNITION IN AFFECTIVE DISORDERS
BD I	BIPOLAR DISORDER
BD II	BIPOLAR II DISORDER
CI	CONFIDENCE INTERVAL
CRP	C-REACTIVE PROTEIN
CVLT	CALIFORNIA VERBAL LEARNING TEST
DSM-5	DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS, 5TH EDITION
DSST	DIGIT SYMBOL SUBSTITUTION TEST
GAF	GLOBAL ASSESSMENT OF FUNCTIONING
HC	HEALTHY CONTROLS
ICD-10	INTERNATIONAL CLASSIFICATION OF DISEASES, 10TH REVISION
IL	INTERLEUKIN
LTP	LONG-TERM POTENTIATION
MLR	MONOCYTE LYMPHOCYTE RATIO
MPV	MEAN PLATELET VOLUME
NLR	NEUTROPHIL LYMPHOCYTE RATIO
OR	ODDS RATIO
PGIMS	PGI MEMORY SCALE
PLR	PLATELET LYMPHOCYTE RATIO
SD	STANDARD DEVIATION
TMT A	TRAIL MAKING TEST A
TMT B	TRAIL MAKING TEST B
TNF	TUMOUR NECROSIS FACTOR
VPA	VALPROATE
YMRS	YOUNG MANIA RATING SCALE

ΔDSST	CHANGE IN DIGIT SYMBOL SUBSTITUTION TEST
ΔMLR	CHANGE IN MONOCYTE LYMPHOCYTE RATIO
ΔNLR	CHANGE IN NEUTROPHIL LYMPHOCYTE RATIO
ΔPLR	CHANGE IN PLATELET LYMPHOCYTE RATIO
ΔTMT A	CHANGE IN TRAIL MAKING TEST A
ΔTMT B	CHANGE IN TRAIL MAKING TEST B
ΔTOTAL SCORE OF MEMORY	CHANGE IN TOTAL SCORE OF MEMORY
X2	CHI-SQUARE TEST

ABSTRACT

INTRODUCTION: Bipolar disorderis a complex illness characterized by severe mood disturbances, neuropsychological deficits, immunological and physiological changes, and functional impairments. Evidence highlights that cognitive dysfunction and inflammation significantly contribute to adverse psychosocial outcomes in bipolar disorder. In this case-control study, we examined cognitive functions in patients diagnosed with bipolar disorder, along with Neutrophil-Lymphocyte Ratio (NLR), Platelet-Lymphocyte Ratio (PLR), and Monocyte-Lymphocyte Ratio (MLR) as markers of inflammation, and compared them with healthy controls.

AIM OF STUDY: To examine cognitive functioning and neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR) in individuals with bipolar disorder.

MATERIALS AND METHODS: The study included 100 patients aged 18-65 years diagnosed with bipolar disorder per DSM 5 criteria and 30 age healthy controls of the same age range from the Department of Psychiatry at DMC&H Ludhiana. Evaluations were done at weeks 1, 3, and 16. Cognitive functions were assessed using the PGI memory scale, Trail Making Test A and B, and Digit Symbol Substitution Test. Inflammatory markers (NLR, PLR, and MLR) were measured using complete blood counts.

RESULTS: Patients with bipolar disorder exhibited significant cognitive deficits compared to controls at weeks 1, 3, and 16 (all p=0.001) and elevated inflammatory markers (NLR, MLR, PLR) (p=0.000 to p=0.016). The duration of illness significantly influenced cognitive performance and inflammatory markers (p=0.000 to p=0.004). Negative correlations were found between inflammatory markers and cognitive performance. Gender differences showed higher inflammatory markers in females than in males (p=0.000 to p=0.013). Lithium treatment was associated with higher inflammatory markers compared to sodium valproate (p=0.0001 to p=0.017).

CONCLUSION: Patients with bipolar disorder had notable cognitive impairments affecting executive functions, visual retention, recognition, cognitive processing speed, cognitive flexibility, and visuomotor skills and increased systemic inflammation compared to healthy controls. The duration of illness and gender were significant factors influencing these outcomes and lithium treatment correlated with higher inflammatory markers than sodium valproate.This study highlights the critical role of inflammation in cognitive deficits, suggesting potential therapeutic targets for improving outcomes in bipolar disorder.

Keywords: Bipolar affective disorder, cognitive functioning, NLR, PLR, MLR, mood stabilizer.

TABLE OF CONTENTS

S. NO.	TOPIC	PAGES
I	INTRODUCTION	1-6
II	AIMS AND OBJECTIVES	7
III	REVIEW OF LITERATURE	8-33
IV	MATERIALS AND METHODS	34-39
V	OBSERVATIONS AND RESULTS	40-144
VI	DISCUSSION	145-170
VII	SUMMARY AND CONCLUSIONS	171-177
	BIBLIOGRAPHY	178-197
VIII	APPENDICES – I - PROFORMA - MASTER CHART APPENDICES – II - APPROVAL LETTER OF THESIS PLAN - THESIS PLAN	

LIST OF TABLES

TABLE NO.	TITLE	PAGE NO.
1	DISTRIBUTION OF SUBJECTS ACCORDING TO AGE	40
2	DISTRIBUTION OF SUBJECTS ACCORDING TO GENDER	41
3	DISTRIBUTION OF SUBJECTS ACCORDING TO MARITAL STATUS	42
4	DISTRIBUTION OF SUBJECTS ACCORDING TO EDUCATION	43
5	DISTRIBUTION OF SUBJECTS ACCORDING TO OCCUPATION	45
6	DISTRIBUTION OF SUBJECTS ACCORDING TO FAMILY TYPE	47
7	DISTRIBUTION OF SUBJECTS ACCORDING TO RELIGION	48
8	DISTRIBUTION OF SUBJECTS ACCORDING TO RESIDENTIAL OCCUPANCY	49
9	FAMILY HISTORY OF BIPOLAR DISORDER IN CASES	50
10	DISTRIBUTION ACCORDING TO TYPE OF MOOD STABILIZER IN CASES	51
11	MEAN AGE AND INCOME OF SUBJECTS	52
12	DISTRIBUTION OF CASES ACCORDING TO DURATION OF ILLNESS	54
13	COMPARISON OF COGNITIVE FUNCTIONS OF SUBJECTS AT WEEK 1	55
14	COMPARISON OF COGNITIVE FUNCTIONS OF SUBJECTS AT WEEK 3	57
15	COMPARISON OF COGNITIVE FUNCTIONS OF SUBJECTS AT WEEK 16	59
16	COMPARISON OF TOTAL SCORE OF MEMORY OF SUBJECTS AT WEEKS 1,3 AND 16, AND CHANGE IN	61

	TOTAL SCORE OF MEMORY FROM BASELINE TO WEEKS 3 AND 16	
17	COMPARISON OF DIGIT SYMBOL SUBSTITUTION TEST (DSST) SCORES OF SUBJECTS AT WEEKS 1,3 AND 16 AND CHANGE IN DSST FROM BASELINE TO WEEKS 3 AND 16.	63
18	COMPARISON OF TRAIL MAKING TEST A DURATION OF SUBJECTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO 3 AND WEEK 16.	65
19	COMPARISON OF TRAIL MAKING TEST B DURATION OF SUBJECTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	67
20	DISTRIBUTION OF INFLAMMATORY MARKERS AT WEEK 1.	69
21	DISTRIBUTION OF INFLAMMATORY MARKERS AT WEEK 3	70
22	DISTRIBUTION OF INFLAMMATORY MARKERS AT WEEK 16	71
23	CHANGE IN INFLAMMATORY MARKERS FROM BASELINE TO 3 WEEKS	72
24	CHANGE IN INFLAMMATORY MARKERS FROM BASELINE TO 16 WEEKS	73
25	COMPARISON OF INFLAMMATORY MARKERS AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	74
26	COMPARISON OF TRAIL-MAKING TESTS A AND B AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	76
27	COMPARISON OF TOTAL SCORE OF MEMORY AND MOOD STABILIZERSAT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	78
28	COMPARISON OF DIGIT SYMBOL SUBSTITUTION	80

	TEST (DSST) AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	
29	COMPARISON OF TMT A AND TMT B (TRAIL-MAKING TEST) DURATION BETWEEN FEMALE AND MALE PARTICIPANTSAT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TOWEEKS 3 AND 16.	82
30	COMPARISON OF TOTAL SCORE OF MEMORY BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	84
31	COMPARISON OF DIGIT SYMBOL SUBSTITUTION TEST (DSST) BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	86
32	COMPARISON OF MARKERS OF INFLAMMATION BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	88
33	IMPACT OF DURATION OF ILLNESS ON TMT A AND TMT B DURATION (TRAILMAKING TEST)AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	90
34	IMPACT OF DURATION OF ILLNESS ON TOTAL SCORE OF MEMORY AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	92
35	IMPACT OF DURATION OF ILLNESS ON DIGIT SYMBOL SUBSTITUTION TEST (DSST) AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	94
36	IMPACT OF DURATION ILLNESS ON INFLAMMATORY MARKERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	96

37(A)	CORRELATION OF AGE, DURATION OF ILLNESS AND COGNITION	98
37(B)	CORRELATION OF AGE, DURATION OF ILLNESS AND COGNITION	99
38(A)	CORRELATION OF AGE, DURATION OF ILLNESS AND INFLAMMATORY MARKERS	104
38(B)	CORRELATION OF AGE, DURATION OF ILLNESS AND INFLAMMATORY MARKERS	105
39 (A)	CORRELATION OF INFLAMMATORY MARKERS AND TMTA (TRAIL MAKING TEST)	108
39 (B)	CORRELATION OF INFLAMMATORY MARKERS AND TMTA (TRAIL MAKING TEST)	109
40(A)	CORRELATION INFLAMMATORY MARKERS AND TMT B (TRAIL MAKING TEST)	115
40(B)	CORRELATION INFLAMMATORY MARKERS AND TMT B (TRAIL MAKING TEST)	116
41(A)	CORRELATION OF INFLAMMATORY MARKERS AND TOTAL SCORE OF MEMORY	119
41(B)	CORRELATION OF INFLAMMATORY MARKERS AND TOTAL SCORE OF MEMORY	120
42(A)	CORRELATION OF INFLAMMATORY MARKERS AND DIGIT SYMBOL SUBSTITUTION TEST (DSST)	124
42(B)	CORRELATION OF INFLAMMATORY MARKERS AND DIGIT SYMBOL SUBSTITUTION TEST (DSST)	125

LIST OF FIGURES

FIG NO.	TITLE	PAGE NO.
1	DISTRIBUTION OF SUBJECTS ACCORDING TO AGE	40
2	DISTRIBUTION OF SUBJECTS ACCORDING TO GENDER	41
3	DISTRIBUTION ACCORDING TO MARITAL STATUS	42
4	DISTRIBUTION ACCORDING TO EDUCATION	43
5	DISTRIBUTION ACCORDING TO OCCUPATION	46
6	DISTRIBUTION ACCORDING TO FAMILY TYPE	47
7	DISTRIBUTION ACCORDING TO RELIGION	48
8	DISTRIBUTION OF SUBJECTS ACCORDING TO RESIDENTIAL OCCUPANCY	49
9	FAMILY HISTORY OF BIPOLAR DISORDER IN CASES	50
10	DISTRIBUTION ACCORDING TO TYPE OF MOOD STABILIZER IN CASES	51
11(A)	MEAN AGE OF CASES AND CONTROLS	52
11(B)	MEAN INCOME OF CASES AND CONTROLS	53
12	DISTRIBUTION OF CASES ACCORDING TO DURATION OF ILLNESS	54
13	COMPARISON OF COGNITIVE FUNCTION OF CASES AND CONTROLS AT WEEK 1	55
14	COMPARISON OF COGNITIVE FUNCTION OF CASES AND CONTROLS AT WEEK 3	58
15	COMPARISON OF COGNITIVE FUNCTION OF CASES AND CONTROLS AT WEEK 16	60
16	COMPARISON OF TOTAL SCORE OF MEMORY OF SUBJECTS, AND THE CHANGE FROM BASELINE TO WEEK 3 AND WEEK 16	62
17	COMPARISON OF DIGIT SYMBOL SUBSTITUTION TEST (DSST) SCORES OF SUBJECTS AT WEEKS 1,3	64

	AND 16 AND CHANGE IN DSST FROM BASELINE TO WEEKS 3 AND 16.	
18	COMPARISON OF TRAIL-MAKING TEST A DURATION OF SUBJECTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEK 3 AND WEEK 16.	66
19	COMPARISON OF TRAIL MAKING TEST B DURATION OF SUBJECTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	68
20	DISTRIBUTION OF INFLAMMATORY MARKERS AT WEEK 1.	69
21	DISTRIBUTION OF INFLAMMATORY MARKERS AT WEEK 3	70
22	DISTRIBUTION OF INFLAMMATORY MARKERS AT WEEK 16	71
23	CHANGE IN INFLAMMATORY MARKERS FROM BASELINE TO 3 WEEKS	72
24	CHANGE IN INFLAMMATORY MARKERS FROM BASELINE TO 16 WEEKS	73
25	COMPARISON OF INFLAMMATORY MARKERS AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	75
26	COMPARISON OF TRAIL-MAKING TESTS A AND B AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	77
27	COMPARISON OF TOTAL SCORE OF MEMORY AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	79
28	COMPARISON OF DIGIT SYMBOL SUBSTITUTION TEST (DSST) AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	81

29	COMPARISON OF TMT A AND TMT B (TRAIL-MAKING TEST) DURATION BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	83
30	COMPARISON OF TOTAL SCORE OF MEMORY BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	85
31	COMPARISON OF DIGIT SYMBOL SUBSTITUTION TEST (DSST) BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	87
32	COMPARISON OF MARKERS OF INFLAMMATION BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	89
33	IMPACT OF DURATION OF ILLNESS ON TMT A (TRAIL MAKING TEST) AND TMT B DURATION AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	91
34	IMPACT OF ILLNESS DURATION ON TOTAL SCORE OF MEMORY AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	93
35	IMPACT OF ILLNESS DURATION ON DIGIT SYMBOL SUBSTITUTION TEST (DSST) AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	95
36	IMPACT OF ILLNESS DURATION ON INFLAMMATORY MARKERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.	97
37 (A)	CORRELATION OF AGE AND TRAIL MAKING TEST A	100
37(B)	CORRELATION OF AGE AND TRAIL MAKING TEST B	100

37(C)	CORRELATION OF AGE AND TOTAL SCORE OF MEMORY	101
37(D)	CORRELATION OF DURATION OF ILLNESS ND TMT A (TRAIL MAKING TEST A)	102
37(E)	CORRELATION OF DURATION OF ILLNESS AND TMT B (TRAIL MAKING TEST B)	102
37(F)	CORRELATION OF DURATION OF ILLNESS AND DIGIT SYMBOL SUBSTITUTION TEST SCORES	103
38(A)	CORRELATION OF DURATION OF ILLNESS AND NLR.	106
38(B)	CORRELATION OF DURATION OF ILLNESS AND MLR.	106
38(C)	CORRELATION OF DURATION OF ILLNESS AND PLR.	107
39(A)	CORRELATION OF TMT A AT WEEK 1 AND PLR AT WEEKS 1,3 AND 16	110
39(B)	CORRELATION OF TMT A AT WEEK 1 AND NLR AND MLR AT WEEKS 1,3 AND 16	110
39(C)	CORRELATION OF TMT A AT WEEK 3 AND PLR AT WEEKS1, 3 AND 16	111
39(D)	CORRELATION OF TMT A AT WEEK 3 AND NLR, MLR AT WEEKS 1, 3 AND 16	111
39(E)	CORRELATION OF TMT A AT WEEK 16 AND NLR AND MLR AT WEEKS 1, 3 AND 16	112
39(F)	CORRELATION OF TMT A AT WEEK 16 AND PLR AT WEEKS 1, 3, AND 16	112
39(G)	CORRELATION OF CHANGE IN TMT A FROM BASELINE TO 3 WEEKS AND NLR AND MLR AT WEEKS1, 3 AND 16	113
39(H)	CORRELATION OF CHANGE IN TMT A FROM BASELINE TO 3 WEEKS AND PLR AT WEEKS 1, 3, AND 16	113
39(I)	CORRELATION OF CHANGE IN TMT A FROM BASELINE TO 16 WEEKS AND NLR AND MLR AT WEEKS 1,3 AND 16	114

39(J)	CORRELATION OF CHANGE IN TMT A FROM BASELINE TO 16 WEEKS AND PLR AT WEEK 1, 3, AND WEEK 16	114
40(A)	CORRELATION OF CHANGE IN TMT B FROM BASELINE TO 3 WEEKS AND MLR AT WEEKS 1,3 AND 16	117
40(B)	CORRELATION OF CHANGE IN TMT B FROM BASELINE TO 16 WEEKS AND MLR AT WEEKS 1, 3, AND 16	117
40(C)	CORRELATION OF CHANGE IN TMT B FROM BASELINE TO 16 WEEKS AND PLR AT WEEKS 1, 3, AND 16	118
41(A)	CORRELATION OF TOTAL SCORE OF MEMORY AT WEEK 1 AND NLR AT WEEK 1, WEEK 3 AND WEEK 16	121
41(B)	CORRELATION OF CHANGE IN TOTAL SCORE OF MEMORY FROM BASELINE TO WEEK 16 AND NLR AT WEEK 1, WEEK 3, AND WEEK 16	122
41(C)	CORRELATION OF CHANGE IN TOTAL SCORE OF MEMORY FROM BASELINE TO WEEK 16 AND MLR AT WEEK 1, WEEK 3, AND WEEK 16	122
41(D)	CORRELATION OF CHANGE IN TOTAL SCORE OF MEMORY FROM BASELINE TO WEEK 16 AND CHANGE IN NLR FROM BASELINE TO WEEK 3 AND WEEK 16	123
42(A)	CORRELATION OF DSST AT WEEK 1 AND NLR AT WEEK 1, 3 AND 16	126
42(B)	CORRELATION OF DSST AT WEEK 1 AND MLR AT WEEKS 1, 3 AND 16	126
42(C)	CORRELATION DSST AT WEEK 1 AND PLR AT WEEKS 1, 3 AND 16	127
42(D)	CORRELATION OF DSST AT WEEK 3 AND NLR AT WEEK 1, 3 AND 16	127

42(E)	CORRELATION OF DSST AT WEEK3 AND MLR AT WEEK 1, 3, AND 16	128
42(F)	CORRELATION OF DSST AT WEEK3 AND PLR AT WEEK 1, 3, AND 16	128
42(G)	CORRELATION OF DSST AT WEEK 16 AND NLR AT WEEK 1, 3 AND 16	129
42(H)	CORRELATION OF DSST AT WEEK 16 AND MLR AT WEEK 1, 3, AND 16	129
42(I)	CORRELATION OF DSST AT WEEK 16 AND PLR AT WEEK 1, 3, AND 16	130

BABA FARID UNIVERSITY OF HEALTH SCIENCES
Sadiq Road, Faridkot-151203 (Pb.) INDIA
Phone No. 91-1639-256253 and Fax No. 91-1639-256234
Website: www.bfuhs.ac.in, Email: bfuhspc@gmail.com
(BFUHS – UNIVERSITY LIBRARY- Coordinator APC)

11-BFUHS (LI-PC-134)24/734 Dated: July 09, 2024

Plagiarism Verification Certificate

Title of the thesis: **Cognitive Functioning and Neutrophil Lymphocyte Ratio (NLR), Platelet Lymphocyte Ratio (PLR) and Monocyte Lymphocyte Ratio (MLR) in Bipolar Affective Disorder.**

Total Page: **124 (One Hundred Twenty Four only) eFSPC (eFile Sent for Plagiarism Check)**

Researcher: **Sandeep Kaur Dhillon**

Supervisor: **Dr. Navkiran Sooch Mahajan**

Co-Supervisor: **Dr. Ranjive Mahajan & Dr. Bhavna Malhotra**

Research Centre: **Dayanand Medical College & Hospital, Ludhiana**

This is to report that the above thesis was scanned for similarity detection. Process and outcome is given below:

DID:	**2093750**	Software used:	**DRILLBIT**
Date:	**July 09, 2024**	Similarity Index:	**4% (Below 10 Percent)**

Total words count: **31844 (eFSPC)**

The complete report is submitted for review by the Supervisor and Co-Supervisor.

University Coordinator/
Name & Signature (Checked by)
(From University library)

The complete report of the above thesis has been reviewed by the undersigned. (Check Box)

☐ The similarity index is below accepted norms.

☐ The similarity index is above accepted norms, because of the following reasons:

1.....
2.....
3…….....
4…….....
5……

The thesis may be considered for the award of degree. (Relevant documents attached).

Research Scholar **Co-Supervisor** **Supervisor**

INTRODUCTION

Bipolar and related disorders encompass bipolar I disorder (BD-I), bipolar II disorder (BD-II), cyclothymic disorder, other specified bipolar and related disorders, and unspecified bipolar or related disorders. In the International Classification of Diseases 10th Revision (ICD-10), the term "bipolar affective disorders" was updated to "bipolar disorders" in the ICD-11. The ICD-11 section on bipolar disorders is titled "bipolar and related disorders," aligning with the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) [1].

Bipolar disorder (BD) is a chronic psychiatric condition marked by alternating hypomanic/manic and major depressive episodes. It is a severe and persistent mental illness characterized by mood disturbances, including (hypo) mania or depression, and variations in physical activity [2]. Globally, BD affects 2–3% of the population, typically beginning around 20 years of age [3]. BD is a significant factor in worldwide disability [4], with patients experiencing high rates of premature mortality due to suicide and co morbid conditions such as cardiovascular disease, diabetes mellitus, and chronic obstructive pulmonary disease (COPD) [2,5]. The disorder shows two onset peaks: 15-24 years and 45-54 years, with over 70% of individuals displaying clinical symptoms before 25 [6][7]. BD occurs relatively equally across sex, ethnicity, and in both urban and rural areas [8][9].

The Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) categorizes BD into three main types: BD type I, BD type II, and cyclothymic disorder [10]. BD type I patients have experienced at least one manic episode (an abnormally elevated mood or irritability with severe functional impairment or psychotic symptoms for seven days or more), with or without major depressive episodes. BD type II patients have experienced at least one hypomanic episode (an abnormally elevated mood or irritability with altered function for four days) and one major depressive episode [10].

Cognitive deficits are impairments in cognitive abilities tied to the functioning of specific brain regions, neural pathways, or cortical networks [11]. Research indicates that neurocognitive deficits are prevalent in severe mental illnesses, including bipolar disorder. These deficits are present in addition to the primary symptoms of the disorder [12,13].

Neurocognitive deficits in bipolar disorder have been extensively documented, affecting executive functioning, verbal and visual memory, attention, and visuospatial abilities [12,14]. Some deficits are influenced by the patient's current mood state, while others persist even during euthymic periods [12,15].

Studies have identified cognitive impairments in selective attention, attention maintenance, recall and recognition memory, verbal learning, verbal fluency, reaction time, psychomotor functions, and executive functions [16-18]. These impairments are found across all phases of the disorder, including remission [19, 20]. Additionally, some cognitive deficiencies appear before the onset of illness, during the first episode [22, 23], and in unaffected first-degree relatives of patients [24, 25]. These impairments may develop due to five etiologies: iatrogenicity, duration of active disease, neurodevelopment or neurodegenerative processes, and genetic predisposition [26].

Cognitive dysfunction can impact daily activities and work capabilities [27]. Cognitive functioning is linked to functional outcomes in bipolar disorder and can be utilized in research and clinical interventions to mitigate cognitive and functional impairments. Although cognitive function assessments are not commonly conducted in clinical settings, there is an increasing focus on cognitive symptoms within comprehensive treatment plans. Addressing neurocognitive impairment as a therapeutic target is crucial for improving psychosocial functioning and quality of life for patients with BD [28].

Bipolar disorder is a complex and multifactorial condition, influenced by genetic and environmental factors. Recently, there has been growing interest in the function of the immune system and inflammatory pathways in the etiology of BD [29, 30]. Immune and inflammatory imbalances can affect mental functioning from the initial stages of neural development [31,32]. Chronic inflammation is linked to the onset and progression of BD, supporting this notion [33]. Additionally, adjunctive anti-inflammatory treatments can alleviate BD symptoms during various mood episodes [34-36]. For example, N-acetylcysteine, pioglitazone, minocycline, and coenzyme Q10 have shown promising antidepressant effects. Conversely, although evidence is limited, the nonsteroidal anti-inflammatory drug celecoxib may have antimanic effects [34].

A recent meta-analysis revealed significantly higher levels of chemokines (a subset of cytokines that promote directed chemotaxis to sites of inflammation or injury) in patients with BD compared to controls [37]. Notably, elevated chemokine levels were observed even during the euthymic phase, indicating that these inflammatory mediators might serve as enduring markers of the disease [38]. Additionally, a systematic review observed a reduction in anti-inflammatory cytokines and a rise in pro-inflammatory cytokines among BD patients, especially during manic and depressive episodes, further supporting the connection between inflammation and acute phases of BD [39]. It is crucial to note that changes in inflammatory pathways are not confined to peripheral markers; evidence of brain excitotoxicity and inflammation in BD patients has been documented both in vivo [40] and post-mortem [41].

The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR) have recently emerged as proposed inflammatory markers. These ratios are cost-effective, reproducible tests easily derived from standard blood samples collected under simple laboratory conditions. They have been linked to mood disorders, supporting the inflammatory hypothesis in

the etiopathogenesis of these conditions [42]. Numerous studies have explored the potential of NLR, PLR, and MLR as biomarkers for BD. For instance, Çakir et al. [43]discovered that NLR was notably higher in BD patients compared to healthy controls. Other research has focused on specific mood episodes, reporting increased NLR and PLR values [44] and decreased MLR values [45] in manic patients relative to healthy subjects. Kalelioglu et al. observed elevated NLR and PLR levels in BD patients compared to controls, with no notable differences between euthymic and manic phases [46]. Elevated NLR in bipolar patients has also been associated with cognitive impairments, particularly in attention [47].

Additionally, a study suggested a correlation between the lethality of suicide attempts and various biological parameters, including hematological markers. The authors reported higher mean platelet volume and PLR in high-lethality suicide attempters [48]. Ekinci et al. examined blood cell inflammatory ratios in depressed patients with and without suicide attempts, proposing that NLR might be a trait marker for suicidal vulnerability in depression [49]. Despite extensive research into the relationship between suicidal behaviors and neuroinflammation, a causal link between the two remains unproven [50].

A meta-analysis by Mazza et al. [51] reviewed the literature on inflammatory markers in BD, finding that individuals with BD exhibited higher NLR and PLR compared to healthy controls. Subgroup analyses revealed significantly elevated NLR and PLR in patients during manic and other bipolar phases, but this significance disappeared when considering only euthymic bipolar subjects. Notably, only one study in the review assessed MLR [52], which found higher values in bipolar patients than controls. More recently, a cross-sectional study by Mazza et al. compared blood cell inflammation markers across different mood episodes of BD for the first time. The study found higher NLR and MLR in manic episodes compared to depressive episodes, suggesting that

inflammatory changes are particularly pronounced during acute mania [53].

Although the pathophysiology of BD is not fully understood, there is growing evidence supporting the role of inflammation [44,46,54,55]. A recent systematic review found higher levels of interleukin-8 (IL-8), monocyte-chemoattractant protein-1 (MCP-1), eotaxin-1, and interferon-γ-induced protein 10 (IP-10) in BD patients compared to healthy controls [37]. Additionally, variations in serum levels of cytokines such as interleukin-1 (IL-1), IL-2, IL-4, IL-6, tumor necrosis factor (TNF)-alpha, soluble TNF receptor 1, and soluble IL-2 receptor [38,56], as well as acute phase reactants like high sensitivity C-reactive protein (hs-CRP) [57], microglia activation [41], and alterations in tryptophan metabolism via the kynurenine pathway [58], have been reported in BD patients.

The neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR) are derived from a complete blood count, an affordable and reliable test widely available in clinical settings. Elevated values of these ratios indicate either neutrophilia or lymphopenia. Numerous studies have reported neutrophilia in patients with BD [59,60] and in those with unipolar depression [61], where lymphopenia is also observed. Consequently, numerous studies have evaluated these ratios in psychiatric conditions, including BD. However, findings are mixed: some studies report elevated NLR in BD patients [43], while others report elevated NLR and PLR regardless of mood state [46]. Studies focusing on specific mood states have shown increased NLR [50] and PLR [44] values, as well as decreased MLR values [45] in manic patients compared to healthy controls. Research examining mood states in BD patients also presents conflicting results, with some studies finding no difference between euthymic and manic phases [46], and others reporting significantly higher NLR, PLR, and MLR in (hypo)manic compared to depressed individuals [62]. A meta-analysis concluded that immune

system activation occurs during mood disorders, with NLR and PLR serving as useful indicators of this activation [51].

Chronic inflammation may contribute to cognitive impairments in bipolar disorder through mechanisms such as microglial activation and impaired neurogenesis. Significant correlations have been observed between cognitive deficits and lower levels of interleukin-7 (IL-7), vascular endothelial growth factor C (VEGF-C), and placental growth factor (PlGF), while higher levels of basic fibroblast growth factor (bFGF) have been linked with better cognitive performance [63].

The current study was undertaken to evaluate the role of markers of inflammation such as NLR, PLR, and MLR, and cognitive functioning in patients with bipolar disorder.

AIMS AND OBJECTIVES

To examine cognitive functioning and neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR) in individuals with bipolar disorder.

Trivedi et al. (2008) investigated cognitive functions in euthymic bipolar disorder patients compared to healthy controls. Using a cross-sectional, case-control design, they assessed 15 euthymic bipolar patients and 15 matched controls with the Wisconsin Card Sorting Test (WCST), Spatial Working Memory Test (SWMT), and Continuous Performance Test (CPT). The study found significant deficits in executive function in the bipolar group, evidenced by more perseverative errors and fewer categories completed in the WCST, indicating that these impairments may be trait markers of bipolar disorder. However, no statistically significant differences were found in attention and working memory. The study's strengths include rigorous selection criteria and robust cognitive assessments, though its small sample size and potential recall bias suggest a need for further research to generalize the findings [28].

A five-year follow-up study by Santos et al. (2014) examined the neurocognitive functioning of 80 euthymic bipolar disorder patients and 40 healthy controls. Neuropsychological assessments at baseline and after five years evaluated six cognitive domains: processing speed, working memory, attention, verbal memory, visual memory, and executive function. The study found that, although both groups maintained stable cognitive performance over time, significant differences in cognitive functioning persisted between the bipolar patients and healthy controls. Bipolar patients showed lower performance across all six domains at both baseline and after five years. The advancement of cognitive dysfunction was similar between the groups in five out of the six areas, but delayed free recall, a measure of verbal memory, declined significantly more in BD patients compared to controls. These findings suggest that cognitive impairment in bipolar disorder is persistent and stable over time, with a particular progressive decline in verbal memory [64].

Pachet AK et al. (2003) [65] conducted a study to synthesize findings from previous research on lithium-associated cognitive impairment across various cognitive domains. The study also examined the "reversibility" of neuropsychological impairment after discontinuing lithium and whether long-term lithium use negatively affects cognition. Despite methodological issues, poor replicability, and the subtle cognitive effects of lithium, five consistent findings emerged: impaired psychomotor speed, impaired verbal memory in most studies, no impairment in visuospatial constructional ability or attention/concentration tasks, and no negative cumulative effect. Many patients on lithium carbonate reported mental slowness. The review indicated that lithium carbonate has definite but subtle negative effects on psychomotor speed and trends toward impaired verbal memory. Recommendations for future research, addressing methodological and statistical problems, and additional clinical implications are provided.

Kim YK et al. (2007) [66] explored the role of cytokines in the pathophysiology of bipolar disorder. The study recruited 37 manic patients and 74 control subjects. Using quantitative sandwich ELISA, they measured the mitogen-induced production of tumor necrosis factor (TNF)-alpha, interleukin-6 (IL-6), IL-4, interferon (IFN)-gamma, and IL-2 at admission and after six weeks of mood stabilizer treatment. Results showed that IL-6 and TNF-alpha production was significantly higher in bipolar manic patients compared to controls, while IL-4 levels were significantly lower. Ratios of IL-6/IL-4, TNF-alpha/IL-4, IL-2/IL-4, and IFN-gamma/IL-4 were significantly elevated in bipolar manic patients. After six weeks of treatment, IL-6 levels significantly decreased from baseline. These findings suggest that increased pro-inflammatory cytokine activity and disparity between pro-inflammatory and anti-inflammatory cytokines could play a role in the pathophysiology of bipolar disorder.

Sagar et al. (2018) [67] conducted a study titled "Assessment of cognitive functions in bipolar I disorder: A 1-year naturalistic follow-up

study," which examined the cognitive functioning of bipolar I disorder (BD-I) patients over one year. The study involved 129 BD-I patients (categorized as manic, depressed, and euthymic) and 49 healthy controls, with cognitive assessments performed at baseline and 3, 6, 9, and 12 months. The findings showed that all patient groups had significant cognitive impairments in areas such as attention, memory, executive functions, and working memory compared to controls at all time points. However, cognitive functions remained largely stable over the year, with slight improvements in specific tests for some groups. Notably, significant group-by-time interactions were observed for executive functions and working memory in depressed patients, visual memory and working memory in manic patients, and working memory in euthymic patients at 12 months.

Bora E et al. (2009) [68] conducted a study to identify neuropsychological deficits linked to genetic susceptibility, the illness process, and iatrogenic factors in bipolar disorder (BD). Through an extensive literature search across multiple databases, meta-analyses were performed on 18 cognitive variables in studies comparing the performance of euthymic BD patients (45 studies; 1423 subjects) or first-degree relatives of BD patients (17 studies; 443 subjects) with healthy controls. Both patient and relative groups exhibited common deficits in response inhibition, set-shifting, executive function, verbal memory, and sustained attention, with medium to large effect sizes for patients and small to medium effect sizes for relatives. Processing speed, visual memory, and verbal fluency deficits were observed only in patients. Medication effects contributed to psychomotor slowing in BD patients. An earlier age of onset was linked to verbal memory impairment and psychomotor slowing. Response inhibition deficit, indicative of ventral prefrontal dysfunction, appears to be a prominent end phenotype of BD. The cognitive endophenotype of BD involves impairments related to front-temporal and front-limbic regions. Processing speed impairment is partially due to medication effects, highlighting the impact of confounding factors rather than genetic

susceptibility. Patterns of sustained attention and processing speed impairments differ from those observed in schizophrenia.

Wingo AP et al. (2009) [69] conducted a comprehensive literature search, initially identifying 586 reports of potential interest. They identified 12 studies involving 276 lithium-treated subjects and 263 comparable lithium-free subjects. Lithium was taken for an average duration of 3.9 years by patients with affective disorders and 2.5 weeks by healthy volunteers, with a mean daily trough serum concentration of 0.80 mEq/L. Overall, lithium treatment was linked with small but significant impairments in immediate verbal learning and memory (effect size (ES) = 0.24; 95% CI, 0.05-0.43) and creativity (ES = 0.33; 95% CI, 0.02-0.64), whereas delayed verbal memory, visual memory, attention, executive function, processing speed, and psychomotor performance were not significantly affected. Among the 326 affective-disorder patients, long-term lithium treatment was also associated with greater impairment in psychomotor performance (ES = 0.62; 95% CI, 0.27-0.97), with no evidence of cognitive improvements. Overall, lithium treatment appears to have only minor negative effects on cognition.

Barbosa IG et al. (2014) [70] investigated the distribution of monocytes and lymphocyte subsets and analyzed Th1/Th2/Th17 cytokines in plasma using flow cytometry. The study recruited 21 BD type I patients and 21 age- and sex-matched controls. The BD patients exhibited increased proportions of monocytes (CD14+). Regarding lymphocyte populations, BD patients showed reduced proportions of T cells (CD3+) and cytotoxic T cells (CD3+CD8+). BD patients also had a higher percentage of activated T CD4+CD25+ cells and a lower percentage of IL-10-expressing Treg cells. These findings provide insight into the mechanisms underlying the chronic low-grade inflammatory profile observed in BD patients.

Çakır U et al. (2015) [71] retrospectively analyzed complete blood counts of 103 non-obese individuals with bipolar disorder (BD) and 126

healthy control subjects. The intensity of the disorder was assessed using the Young Mania Rating Scale (YMRS). The study concluded that the neutrophil-to-lymphocyte ratio (NLR) was higher in female patients compared to female controls (3.2±2.2 vs. 1.7±0.4; p<0.001). Similarly, male patients had a significantly higher NLR than healthy male subjects (3.3±2.4 vs. 2.0±0.7; p<0.001). In BD patients, NLR did not significantly correlate with the severity of the disorder (r=0.052; p=0.204) or the duration of the disorder (r=0.045; p=0.301). The study concluded that patients with BD have significantly elevated NLR compared to healthy controls, suggesting that elevated NLR levels could be implicated in the inflammatory pathophysiology of BD.

Kalelioglu T et al. (2015) [46] examined the role of inflammatory cells and their ratios as markers of inflammation in bipolar disorder. The study included 61 manic patients, 55 euthymic patients, and 54 control subjects. Results showed that both neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios were significantly higher in manic and euthymic patients compared to the control group. These findings indicate that inflammatory cells play a role in the pathophysiology of bipolar disorder, both during manic episodes and in the euthymic state.

The study titled "Neuropsychological impairment in bipolar affective disorder" by Taj M. and Padmavati R.[72] examined cognitive dysfunctions in patients with BD who were in remission. This research included 30 bipolar patients and 30 matched healthy controls, assessing neuropsychological functions such as attention, memory, and executive function. The results demonstrated significant impairments in the bipolar group across various tests, including the digit-symbol test, trail-making tests (Parts A and B), digit span forward test, and visual design reproduction test. These cognitive deficits were present despite the patient being in a euthymic state, emphasizing persistent cognitive challenges that can lead to social and occupational difficulties, reduced insight, elevated risk of non-adherence, and relapse.

Rosenblat JD et al. (2019) [34] conducted a systematic review that encompassed a total of 555 BD subjects to assess the relationship between cognitive function and inflammatory markers. The review found that cognitive dysfunction was linked to increased levels of pro-inflammatory markers such as YKL40, IL-6, sCD40L, IL-1Ra, hsCRP, and TNF-α. Mechanistically, increases in inflammatory cytokines can alter monoamine levels, leading to cognitive and affective dysfunction. Neuro-inflammation, evidenced by microglial activation, results in increased oxidative stress, pathological synaptic pruning, and impaired neuroplasticity in key brain regions involved in mood and cognition. Additionally, immune dysfunction can activate the hypothalamic-pituitary-adrenal (HPA) axis, leading to hypercortisolemia and metabolic dysfunction, further promoting neuronal dysfunction. Anti-inflammatory agents are currently being investigated for the treatment of BD and appear to have antidepressant effects; however, cognitive outcomes have not yet been reported. Several studies indicate that immune dysfunction is linked to cognitive impairment in BD, with multiple neurobiological pathways identified through which immune dysfunction may contribute to cognitive deficits in BD.

Bauer IE et al. (2015) [73] evaluated cognitive performance in bipolar disorder (BD) patients using the Brief Assessment of Cognition in Affective Disorders (BAC-A), a specialized test battery designed for BD, to determine its effectiveness in estimating global functioning. The study involved 93 BD patients (mean age ± SE: 35.18±1.39 years) and 56 healthy controls (HC; mean age ± SE: 36.17±1.91 years). The BAC-A scores were summarized into eight categories: visuomotor, immediate affective and non-affective memory, verbal fluency, delayed affective and non-affective memory, inhibition, and problem-solving. Post hoc analyses were conducted on subtests that showed significant differences between BD patients and HC. Correlational analyses examined the relationship between the Global Assessment of Functioning (GAF) score and cognitive performance. BD patients demonstrated significant impairments in short-term non-affective

memory and verbal fluency compared to HC. Reduced performance in verbal memory and verbal fluency scores was positively correlated with lower GAF scores. These findings align with previous reports of verbal memory and verbal fluency deficits in BD. The impairments in short-term memory and semantic fluency may reflect inefficient learning strategies and/or difficulties in information retrieval. The BAC-A could potentially be used to estimate global functioning in BD patients.

Bhatia P et al. (2018) [11] investigated cognitive impairments in 60 euthymic bipolar disorder (BPAD) patients using the NIMHANS neuropsychological battery and compared their performance to normative data. The study found that about half of the patients exhibited significant cognitive impairments in mental speed, sustained attention, verbal fluency, working memory, set-shifting, verbal and visual memory, and visuoconstructional ability. The duration of illness and the number of episodes had a significant correlation with impairments in psychomotor performance, attention, and executive function. Residual depressive and manic symptoms further contributed to deficits in specific cognitive domains. Additionally, different medication regimens, particularly when lithium and atypical antipsychotics when combined, were associated with varying levels of cognitive dysfunction.

Bora E et al. (2015) [74] conducted a meta-analytic review comparing neurocognitive deficits in first-episode bipolar (FEBP) patients and healthy controls and first-episode schizophrenia (FES) patients. The meta-analysis included 22 adult studies, encompassing 533 FEBP patients, 1417 healthy controls, and 605 FEBP and 822 FES patients. FEBP patients showed significant impairments across all cognitive domains (effect size (d) = 0.26–0.80) and individual tasks (d = 0.22–0.66). FES patients performed significantly worse than FEBP patients in most cognitive domains (d = 0.05–0.63) and on individual tasks (d = 0.13–0.77). Neuropsychological impairment in FEBP was comparable to that seen in chronic bipolar disorder, with cognitive functions in

FEBP falling between those of FES patients and healthy controls. These findings indicate that neurodevelopment factors play a significant role in both schizophrenia and bipolar disorder.

Demant KM et al. (2015) [75] investigated the relationship between global and domain-specific objective and subjective cognitive function, as well as the association between global cognitive function and psychosocial functioning. The study also aimed to identify clinical variables that predict objective and subjective cognitive function and psychosocial functioning. They found a correlation between global subjective and objective measures of cognitive dysfunction, but not within individual cognitive domains. However, the correlation was weak, indicating that cognitive complaints do not directly reflect actual cognitive performance. Self-reported psychosocial difficulties were associated with subjective (but not objective) cognitive impairment, and both subjective cognitive and psychosocial difficulties were predicted by depressive symptoms. These findings suggest that effective assessment of cognition in clinical treatment and drug trials for BD should include both subjective measures and objective neuropsychological tests.

Sayana P et al. (2017) [39] conducted a systematic review to analyze inflammatory markers in human studies, focusing on each marker's potential clinical application and summarizing evidence of their role in bipolar disorder (BD). The review included studies on peripheral markers, genetic analyses, post-mortem examinations, and cell studies involving inflammatory biomarkers in BD. A total of 102 papers met the inclusion criteria. The review found that pro-inflammatory cytokines were elevated and anti-inflammatory cytokines were reduced in BD patients, particularly during manic and depressive phases, compared to controls. These inflammatory changes tended to subside during euthymia, suggesting that inflammation is associated with the acute phases of BD.

Özdin S et al. (2017) [76] compared NLR, PLR, MLR, and complete blood count elements in patients treated and hospitalized for schizophrenic psychotic episodes and bipolar disorder manic episodes. The study included all patients meeting the inclusion criteria who were receiving treatment and hospitalized for either schizophrenia-psychotic episodes or bipolar affective disorder-manic episodes. A total of 157 healthy donors served as the control group. White blood cell (WBC), neutrophil, lymphocyte, platelet, and monocyte counts were retrospectively obtained from complete blood counts at the time of admission, and NLR, PLR, and MLR were calculated. The study found that BD patients had increased NLR, PLR, and MLR values, platelet counts, and lower lymphocyte counts compared to controls. Similarly, schizophrenia patients exhibited higher NLR, PLR, MLR values, neutrophil counts, and lower lymphocyte counts compared to controls. Schizophrenia patients had higher NLR and MLR values compared to BD patients.

Goyal et al. (2023) [77] conducted a study titled "Comparison of NLR (neutrophil/lymphocyte ratio) and PLR (platelet/lymphocyte ratio) as inflammatory markers in 1st episode mania and bipolar mania," which assessed and compared these inflammatory markers in 40 bipolar mania patients, 40 drug-naïve first episode mania patients, and 40 healthy controls. The research revealed significantly elevated neutrophil counts and NLR, alongside notably reduced lymphocyte counts in both patient groups compared to controls. Additionally, the first-episode mania group exhibited even higher neutrophil counts and NLR than the bipolar mania group, suggesting that psychotropic medications might exert an anti-inflammatory effect. However, no significant differences in platelet counts and PLR were observed among the groups.

Köhler O et al. (2017) [78] executed two trials on comparative effectiveness, namely the Clinical and Health Outcomes Initiatives in Comparative Effectiveness for Bipolar Disorder Study (Bipolar

CHOICE) and the Lithium Treatment Moderate-Dose Use Study (LiTMUS), involving individuals with bipolar disorder. At the commencement of the study, evaluations of white blood cell count and severity of bipolar mood symptoms were performed using the Montgomery-Asberg Depression Rating Scale and the Bipolar Inventory of Symptoms Scale. In the Bipolar CHOICE study with 482 participants, each increase of 1.0 × 10^9/L in white blood cell count significantly correlated with elevated overall symptom severity on the Bipolar Inventory of Symptoms Scale in males (coefficient = 2.13; 95% CI = 0.46-3.79; p = 0.013), but this was not the case for females (coefficient = 0.87; 95% CI = -0.87-2.61; p = 0.33). Interaction analysis indicated a possible trend towards increased symptom severity in males (coefficient = 1.51; 95% CI = -0.81-3.82; p = 0.2). In the LiTMUS study with 283 participants, higher fluctuations from the median white blood cell count were associated with a tendency towards higher scores on the Montgomery-Asberg Depression Rating Scale in males (coefficient = 1.33; 95% CI = -0.22-2.89; p = 0.09), but not in females (coefficient = 0.34; 95% CI = -0.64-1.32; p = 0.50). When data from both LiTMUS and Bipolar CHOICE were combined, scores on the Montgomery-Asberg Depression Rating Scale significantly increased with each 1.0 × 10^9/L rise in white blood cell count in males (coefficient = 1.09; 95% CI = 0.31-1.87; p = 0.006), with a less pronounced correlation in females (coefficient = 0.55; 95% CI = -0.20-1.29; p = 0.14). Fluctuations in white blood cell levels, even within normal limits, were linked to higher mood symptom severity in bipolar disorder, particularly among men.

Bora E and Özerdem A (2017) [79] conducted a meta-analysis to examine longitudinal neurocognitive changes in bipolar disorder (BP) and to compare the trajectory of cognitive deficits in BP with schizophrenia and healthy controls. The meta-analysis included a total of 22 reports. The findings indicated no cognitive decline over time in either short-term (mean duration = 1.5 years) or long-term (mean duration = 5.5 years) follow-up studies in BP. Instead, there was

evidence of modest improvements in task performance related to memory and working memory at follow-up. The trajectory of cognitive functioning in BP was not significantly different from changes observed in schizophrenia and healthy subjects. These results, along with findings in early BP and individuals at genetic risk for BP, suggest that neurodevelopmental factors may play a significant role in cognitive deficits in BP and do not support the idea of progressive cognitive deterioration in most patients with BP.

Sağlam Aykut D et al. (2018)[47] investigated the impact of inflammatory markers on cognitive functions in euthymic patients with bipolar disorder. The study included 28 patients with type-I bipolar disorder and 22 healthy controls matched for age, gender, and educational status. Neuropsychological tests were administered to all participants. Neutrophil, lymphocyte, and platelet counts were measured, and neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) were calculated. The study found a significant negative correlation between NLR and Strop interference scores in the bipolar disorder group. However, there was no statistically significant difference in NLR and PLR between the study and control groups, and no significant correlation was found between PLR and neurocognitive test scores. This study revealed a negative correlation between NLR and Stroop interference scores in bipolar disorder patients.

Keshri et al. (2018) [80] conducted a study titled "Elevated interleukin-17 and reduced testosterone in bipolar disorder. Relation with suicidal behavior," which investigated the relationship between interleukin-17 (IL-17), testosterone levels, and suicidal behavior in bipolar disorder (BD). The case-control study encompassed 41 male bipolar disorder patients in remission and 41 age-matched healthy controls. The findings revealed that IL-17 levels were notably higher and testosterone levels were notably lower in BD patients in comparison to controls. Additionally, IL-17 levels were negatively correlated with testosterone levels and positively correlated with the duration of illness

in BD patients. However, neither IL-17 nor testosterone levels were significantly linked with suicidal behavior within the BD group. These results suggest that elevated IL-17 and reduced testosterone levels may be linked to the pathophysiology and progression of BD, but not directly to suicidal behavior.

Mazza MG et al. (2018) [51] identified 11 studies from major electronic databases that met their inclusion criteria. Meta-analyses were conducted, generating pooled standardized mean differences (SMDs) between bipolar disorder (BD) subjects and healthy controls (HC). BD subjects had higher NLR and PLR compared to HCs (SMD = 0.672; $p < 0.001$; $I2 = 82.4\%$ and SMD = 0.425; $p = 0.048$; $I2 = 86.53\%$, respectively). Subgroup analysis showed that the bipolar phase influenced the overall estimate, with studies including subjects in manic or any bipolar phase showing notably higher NLR and PLR compared to HCs, whereas the effect was not significant in studies including only euthymic bipolar subjects. Meta-regression indicated that age and gender influenced the association between BD and NLR, but not the association between BD and PLR. A meta-analysis for MLR was not conducted because only one study compared BD to HC and one study compared major depressive disorder (MDD) to HC. MDD subjects had higher NLR compared to HCs (SMD = 0.670; $p = 0.028$; $I2 = 89.931\%$). Heterogeneity-based sensitivity analyses and meta-regression confirmed these findings. This meta-analysis supports the hypothesis that inflammatory activation occurs in mood disorders and that NLR and PLR could be useful indicators of this activation.

Inanli I et al. (2019) [55] conducted a retrospective study to compare neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), and mean platelet volume (MPV) in depressive, manic, and euthymic bipolar disorder (BD) patients against healthy controls, aiming to determine whether these values could serve as state or trait biomarkers for BD. The study included 341 BD patients (100 depressive, 141 manic, and 100

euthymic) and 114 healthy controls. The results indicated that manic BD patients had elevated levels of MPV, NLR, and MLR, while depressive BD patients had higher MPV levels compared to controls. MPV was a predictor for all BD states, whereas NLR and MLR specifically predicted the manic state. These findings suggest that NLR, MLR, and MPV, derived from simple and cost-effective blood tests, are significantly higher in BD patients compared to healthy controls, indicating low-grade inflammation. MPV may serve as a potential trait biomarker for BD, while NLR and MLR may serve as state biomarkers for the manic phase.

Kirlioglu SS et al. (2019) [81] investigated the inflammatory status differences between bipolar patients in manic and mixed episodes by measuring NLR, PLR, and MLR levels. The study included 48 bipolar patients experiencing a mood episode (28 manic, 20 mixed) and 32 controls. Data on sociodemographic and clinical variables, along with laboratory findings, were collected for all participants. Red cell distribution width (RDW), mean platelet volume (MPV), neutrophil, lymphocyte, and platelet count, NLR, PLR, and MLR were recorded. The results showed that PLR and MLR were significantly higher in bipolar patients compared to controls, while NLR and MLR were significantly higher in manic patients than in mixed patients. RDW was higher in mixed episode patients compared to controls. These findings suggest that MLR could be considered a novel state biomarker for bipolar mood episodes, with greater inflammatory activation in mania compared to mixed episodes.

Melo MCA et al. (2019) [82] examined the clinical implications of NLR and PLR in bipolar disorder (BD) patients in an 18-month prospective study that followed 80 euthymic BD outpatients. Baseline data included an interviewer-administered questionnaire, behavioral scales, and a blood count to calculate NLR and PLR. Mood episodes and hospitalizations were assessed monthly for 18 months. Higher NLR and PLR were associated with increased anxiety symptoms and poorer

functioning. BD patients with Night Eating Syndrome (NES) had higher PLR and tended toward higher NLR. Additionally, higher NLR and PLR were linked to more episodes and hospitalizations over the 18 months, with higher baseline NLR specifically related to more (hypo)manic episodes. This study highlighted the predictive significance of NLR and PLR in BD, suggesting the utility of a simple blood count in evaluating BD progression.

Lin X et al. (2019) [83] conducted a study to compare subjective cognitive functioning and explore associations between subjective and objective cognitive functioning across different BD clinical states while investigating the roles of mood symptoms in predicting and moderating these associations. The study assessed subjective cognitive functioning (using the Cognitive Complaints in Bipolar Disorder Rating Assessment, COBRA) and several domains of cognitive functioning (using a neuropsychological battery) in 48 hypomanic or manic patients, 42 depressed bipolar patients, 50 euthymic bipolar patients, and 60 healthy controls. All bipolar disorder patient groups exhibited subjective and objective cognitive deficits compared to healthy controls. There was a significant association between subjective and objective cognitive functioning in the euthymic group, but not in the acute symptomatic groups, where mood symptoms moderated the associations. Subjective cognitive functioning was significantly correlated with mood symptoms, with depressive symptoms being the best predictor. These findings suggest that mood symptoms influence the relationship between subjective and objective cognitive dysfunction, underscoring the need for a comprehensive neuropsychological test battery to accurately assess cognitive deficits in clinical settings, regardless of subjective complaints.

Luo X et al. (2020) [84] investigated the prevalence and relevant factors of subjective cognitive functioning and its potential effects on predicting psychosocial functioning and suicidal ideation in bipolar disorder (BD). The study included 92 patients with BD type I (42 depressed and 50

euthymic) and 60 healthy individuals. Participants underwent a battery of neuropsychological tests assessing attention and processing speed, visual memory, working memory, and executive functions, as well as the Cognitive Complaints in Bipolar Disorder Rating Assessment, the Global Assessment of Functioning scale, and the Beck Scale for Suicide Ideation. Results showed that bipolar patients had worse subjective cognitive dysfunction compared to healthy controls, with depressed patients reporting more cognitive complaints than euthymic patients. In the bipolar group, psychosocial functioning, suicidal ideation, and occupational status were the main factors related to subjective cognitive functioning. Subjective cognitive functioning also predicted psychosocial functioning and suicidal ideation. While depressive symptoms moderated the relationship between objective cognitive functioning and suicidal ideation, they did not moderate the correlation between cognitive functioning and psychosocial functioning.

Burdick KE et al. (2020) [85] carried out a systematic evaluation of lithium's impact on neurocognitive functions within the largest single group (n = 262) of BD patients yet, using data from an ongoing, multi-site clinical trial focused on lithium as a sole treatment. At a cross-sectional analysis level, a multivariate analysis of covariance (MANCOVA) assessed potential cognitive differences among groups through various neurocognitive tests (California Verbal Learning Test [CVLT trials 1–5, CVLT delayed recall], Wechsler Digit Symbol, Trail-making Test parts A and B [TMT A; TMT B], and a global cognition index). Longitudinally, for a subset of 88 patients who reached mood stabilization on lithium alone, the study investigated how lithium treatment affected neurocognitive functions over time. Initial assessments showed no differences in neurocognitive performance between BD patients on lithium and those not on the treatment. At the time of follow-up, significant enhancements were noted in global cognitive index scores ($F = 31.69$; $p < 0.001$), CVLT trials 1–5 ($F = 29.81$; $p < 0.001$), CVLT delayed recall ($F = 15.27$; $p < 0.001$), and TMT B ($F = 6.64$; $p = 0.012$). These results indicate that lithium

potentially aids neurocognitive functioning in BD patients and does not substantially hinder cognition when used for treatment.

Pigoni A et al. (2020) [86] conducted a review summarizing the findings of studies that evaluated the impact of valproate on cognition in patients with bipolar disorder (BD). Ten studies met the inclusion criteria, including one double-blind quasi-randomized study and nine cross-sectional or naturalistic studies. These studies either a) used healthy subjects as a control group (N = 1), b) compared valproate-treated patients with healthy individuals and those on other treatments (N = 5), or c) compared valproate-treated patients with those on other treatments, focusing specifically on lithium (N = 3). The results overall suggested that valproate negatively affects cognitive functions in chronically treated BD patients, particularly impacting working memory. These findings imply that valproate might have a detrimental effect on cognitive functions, especially in the working memory domain. However, the limited number of studies available warrants a cautious interpretation of these results.

Fusar-Poli L et al. (2021) [87] recruited 294 patients with BD, including 143 experiencing a (hypo) manic episode and 151 in a depressive phase. Blood samples were collected to perform a complete blood count, and NLR, PLR, and MLR were calculated. The study found that mean values of neutrophils, platelets, mean platelet volume, NLR, PLR, and MLR were significantly higher in (hypo) manic individuals compared to those in a depressive state. Logistic regression analysis indicated that PLR might serve as an independent predictor of (hypo) mania. These altered inflammatory indexes, particularly PLR, may help explain the onset and recurrence of (hypo) manic episodes in BD patients. Given that inflammatory ratios are economical and accessible markers of inflammation, further studies are recommended to better elucidate their role as peripheral biomarkers for mood episodes in BD.

Xiang R et al. (2021) [88] investigated the effects of carbamazepine and sodium valproate on efficacy, cognitive function, and uric acid levels in

epileptic patients experiencing their first generalized seizure. A total of 120 patients were randomly divided into two groups: a carbamazepine group and a sodium valproate group, with 60 patients in each group. Both groups received medication for one year. Changes in clinical efficacy, cognitive function, and blood uric acid levels were compared between the two groups after one year of treatment, and the correlation between blood uric acid and cognitive function was analysed. The study found no significant difference in the overall effective rate among the two groups ($P>0.05$). Cognitive function scores in both groups significantly improved after 6 months and 1 year of treatment compared to before treatment ($P<0.05$), and no significant difference was observed in cognitive function and blood uric acid levels between the groups at baseline, 6 months, and 1 year ($P>0.05$). A significant positive correlation was found between Mini-Mental State Examination (MMSE) scores and blood uric acid levels in patients with epilepsy ($r=0.279$, $P=0.012$). Both carbamazepine and valproate effectively improved cognitive function in patients with first generalized seizure, with similar clinical efficacy. Blood uric acid levels increased after treatment and positively correlated with cognitive function.

Bergamelli E et al. (2021) [89] summarized the results of functional magnetic resonance imaging (fMRI) studies evaluating the impact of lithium's impact on brain functional activity and connectivity in patients with bipolar disorder (BD). A literature search was conducted using the Pub Med database for studies reported in English since 2016. Five fMRI studies in resting-state conditions and six studies during emotional tasks met the inclusion criteria. The evidence generally supports the normalizing effects of lithium on brain activity and connectivity, particularly in prefrontal regions and interconnected areas involved in emotion regulation and processing, regardless of the task used. Lithium treatment showed distinct patterns of activity and connectivity changes compared to other treatments, and these changes were associated with clinical improvement in BD. However, the heterogeneity of study designs, sample selections, and analysis

methods among the examined studies may limit the generalizability of the findings and complicate comparisons.

Cheng Y et al. (2022) [90] performed a meta-analysis involving 2,264 depressed patients and 2,415 controls. The study found that depressed patients had significantly elevated NLR and PLR in comparison to controls (SMD = 0.33, 95% CI: 0.15–0.52, $p < 0.001$ for NLR; and SMD = 0.24, 95% CI: 0.02–0.46, $p < 0.05$ for PLR). While MLR was slightly higher in depressed individuals (SMD = 0.15, 95% CI: −0.26 to 0.55, $p > 0.05$), it was not statistically significant. However, a sensitivity analysis excluding a heterogeneity-causing study revealed a significant effect on MLR (SMD = 0.32, 95% CI: 0.20–0.44). Subgroup analyses demonstrated significant differences in NLR, PLR, and MLR between depressed individuals and control subjects in China, as well as in the age and gender-matched subgroups. Additionally, post-stroke depression (PSD) patients exhibited higher NLR and MLR values than non-PSD patients (SMD = 0.51, 95% CI: 0.36–0.67, $p < 0.001$ for NLR; and SMD = 0.46, 95% CI: 0.12–0.79, $p < 0.01$ for MLR). Meta-regression analysis indicated that the proportion of males in the case group contributed to heterogeneity in NLR measurements ($p < 0.05$). Elevated inflammatory ratios, particularly NLR, were linked to an increased risk of depression, with NLR, PLR, and MLR all higher in depressed patients compared to controls in the China and age-gender-matched subgroups. Gender differences appeared to influence NLR values in depressed patients.

Su M et al. (2022) [91] conducted a meta-analysis that included 2,580 cases and 2,664 controls for NLR, 1,393 cases and 1,370 controls for PLR, and 744 cases and 765 controls for MLR. The pooled analysis indicated that depressed individuals had significantly higher NLR levels compared to healthy controls (SMD = 0.33, 95% CI = 0.15-0.51, $p < 0.001$). This result was confirmed by sensitivity analysis and publication bias testing. Subgroup analyses suggested that the association between depression and NLR might be influenced by

factors such as country, study design, and antidepressant treatment. No significant differences in PLR (SMD = 0.13, 95% CI = -0.04-0.31, p = 0.140) and MLR (SMD = 0.02, 95% CI = -0.24-0.28, p = 0.892) were observed between depressed subjects and controls. This meta-analysis supports the hypothesis that depression is associated with inflammation and suggests that NLR can serve as an indicator of depression.

Marazziti D et al. (2022) [92] examined the potential connections between NLR, PLR, and MLR in mood disorders (MDs) and discussed their broader applicability in clinical research. This review included 35 studies, most of which reported higher values of these inflammatory markers, particularly NLR, in patients with MDs compared to healthy individuals. The increase was especially notable in patients during manic episodes, suggesting these markers could serve as both state and trait indicators. Elevated NLR and PLR levels also appear to be predictive indicators for early identification of post-stroke depression. The review emphasizes the requirement for further research, highlighting that NLR, PLR, and MLR are promising tools for economically and easily detecting inflammatory system activation and potentially evaluating the etiology and progression of MDs. These markers may also provide insights into the relationship between inflammatory and cardiovascular diseases and MDs, with consequences for clinical treatment and treatment strategies.

Dadouli K et al. (2022) [93] conducted a case-control study involving 180 BD patients and 407 healthy controls. The BD patients were hospitalized and included based on specific criteria, with 111 experiencing manic episodes and 69 experiencing depressive episodes. Complete blood count data were collected from their first hospital admission. The study found that BD patients had significantly higher NLR, MLR, and SII index levels compared to healthy controls during both manic ($p < 0.001$) and depressive ($p < 0.001$) episodes. MLR showed a large effect size increase specifically in manic

episodes. Neutrophils and NLR had the highest area under the curve, with cut-offs of 4.38 and 2.15, respectively, in the ROC analysis. Gender-related differences were observed mainly in the SII index, with increased levels in males during manic episodes and in females during depressive episodes compared to healthy controls. The significantly higher NLR, MLR, and SII index in BD patients suggest a heightened inflammatory response in this population.

Wei Y et al. (2022) [94] conducted a retrospective analysis using data retrieved from electronic health records. The study included 16,174 Chinese patients with affective disorders and 6,681 healthy controls. The researchers compared NLR, MLR, PLR, and whole blood count data across different groups and analyzed the factors contributing to the occurrence of MDD and BD. They found that patients with first-episode and recurrent MDD had significantly higher NLRs and MLRs compared to healthy controls. Additionally, BD patients exhibited higher NLRs and MLRs but lower PLRs compared to MDD patients. Further analysis indicated that BD patients in manic episodes had significantly higher NLRs and MLRs than those in depressive episodes or MDD patients. The study identified MLR as a contributing factor for MDD and both NLR and MLR as contributing factors for BD, underscoring the role of systemic inflammation in the pathophysiology of MDD and BD, especially during manic episodes.

In another study by Wei Y et al. (2022) [95], a retrospective, naturalistic, cross-sectional analysis was performed on data from 14,007 Chinese patients with affective disorders, which included 4,801 first-episode MDD patients, 4,098 recurrent MDD patients, 3,444 BD manic episode patients, and 1,664 BD depressive episode patients. The control group consisted of 6,847 healthy subjects. The study compared MPV, PDW, PCT, SII, PLR, PAR, RPR, and albumin levels across different groups and examined the factors contributing to MDD or BD. Significant differences were found in MPV, PDW, PCT, SII, PLR, RPR, and albumin values among the groups. BD manic episode patients had the

highest mean values of MPV and SII, BD depressive episode patients had the lowest mean values of platelet counts and PAR, and MDD patients had the highest mean values of PLR and RDW. The study highlighted that MPV, PDW, and albumin levels were independently correlated with MDD and BD, serving as important predictors for distinguishing these disorders from healthy controls. The findings emphasized that different affective disorders exhibit unique platelet parameter variation patterns, highlighting the significance of platelet parameters and systemic inflammation in the pathophysiology of MDD and BD.

Keramatian K et al. (2022) [96] performed a MEDLINE literature search, identifying 38 relevant systematic reviews and meta-analyses. The current evidence suggests that bipolar disorder (BD) is linked to cognitive impairment across various domains and in all clinical states. However, there is significant cognitive heterogeneity within BD that cannot be accounted for by clinical subtypes, and the neurocognitive impairment patterns in BD overlap with those in other psychiatric conditions such as major depression and schizophrenia. Factors such as residual depressive symptoms, poor clinical course, and a higher number of manic episodes can adversely affect cognitive performance, which is a key predictor of general functioning in BD. Available prospective studies do not support the idea of progressive cognitive decline in BD; some evidence suggests that patients might experience cognitive enhancements following their first manic episode. Additionally, some patients may exhibit pre morbid cognitive abnormalities indicative of an early neurodevelopmental origin. Preliminary results from small-scale studies suggest potential cognitive benefits from interventions such as Cognitive Remediation, erythropoietin, intranasal insulin, lurasidone, mifepristone, repetitive Transcranial Magnetic Stimulation, and transcranial Direct Current Stimulation in BD.

Naseh M et al. (2022) [97] investigated the effects of Valproate (VPA) treatment on synaptic plasticity dysfunction, hippocampal neuronal loss, and spatial memory deficits induced by cerebral ischemia in the middle cerebral artery occlusion (MCAO) model. Thirty-two male Sprague-Dawley rats were randomly assigned to four groups: control, sham, cerebral ischemia with vehicle (MCAO+V), and MCAO+VPA. The right common carotid artery was occluded for 1 hour, and VPA (300 mg/kg) or vehicle was administered intraperitoneally on days 0, 1, 2, and 3 of reperfusion. Seven days after reperfusion, the Morris water maze, passive avoidance, and open field tests were conducted. Hippocampal synaptic plasticity in the CA1 region was assessed through field potential recording, using neuronal Input-Output (I/O) function and paired-pulse ratio (PPR) to evaluate basal synaptic transmission and presynaptic neurotransmitter release probability, respectively. The brains were then analyzed for stereological parameters of CA1 neurons. The results demonstrated that VPA administration significantly reduced total infarct volume and improved spatial learning, memory, fear memory, and anxiety in MCAO rats compared to the MCAO+V group. Additionally, field potential recordings indicated that VPA significantly improved impaired long-term potentiation (LTP) induced by MCAO, without affecting basal synaptic transmission and neurotransmitter release probability. Therefore, it appears that reducing total infarct volume and enhancing LTP through postsynaptic mechanisms are responsible for the observed improvements in MCAO-induced cognitive impairment.

Hung KC et al. (2023) [98] conducted a meta-analysis that included 11 studies published between 2018 and 2023, involving a total of 10,357 patients. The analysis revealed that patients with cognitive impairment (CI) had a higher neutrophil-to-lymphocyte ratio (NLR) than those without CI (mean difference = 0.35, 95% CI: 0.26–0.44, $p < 0.00001$, $I2 = 86\%$). Additionally, pooled results indicated a significant association between high NLR and the risk of CI (odds ratio [OR] = 2.53, 95% CI: 1.67–3.82, $p < 0.0001$, $I2 = 84\%$). The analysis also identified aging

(mean difference = 4.31 years, 95% CI: 2.83–5.8, p < 0.00001, I2 = 92%), diabetes (OR = 1.59, 95% CI: 1.35–1.88, p < 0.00001, I2 = 66%), and hypertension (OR = 1.36, 95% CI: 1.19–1.57, p < 0.00001, I2 = 0%) as significant risk factors for CI. However, there were no significant associations between CI and male gender (OR = 0.84, 95% CI: 0.64–1.11, p = 0.22, I2 = 81%), body mass index (mean = −0.32 kg/m^2, 95% CI: −0.82, 0.18, p = 0.2, I2 = 82%), alcohol consumption (OR = 1.11, 95% CI: 0.95–1.3, p = 1.35, I2 = 0%), or smoking (OR = 0.99, 95% CI: 0.87–1.13, p = 0.86, I2 = 0%). Meta-regression indicated that diabetes and hypertension, but not age, significantly moderated the association between NLR and CI. This meta-analysis established a strong link between elevated NLR and an increased risk of CI, with diabetes and hypertension identified as significant moderating factors in this relationship.

Zeng J et al. (2023) [99] retrospectively analyzed data from 1,160 eligible patients, comprising 918 with unipolar depression and 242 with bipolar depression. The patient data was randomly divided into training (85%) and open test (15%) sets 1,000 times, with average performance metrics reported. The XGBoost model achieved optimal performance on the open-test set using selected biomarkers and clinical features, with an AUC of 0.889, sensitivity of 0.831, specificity of 0.839, and accuracy of 0.863. Feature importance for differential diagnosis was assessed using Shapley additive explanations (SHAP) values. The most informative features included clinical characteristics such as disease duration and age of onset, biochemical markers like albumin, low-density lipoprotein (LDL), and potassium, and complete blood count-derived biomarkers such as white blood cell count (WBC), platelet-to-lymphocyte ratio (PLR), and monocytes (MONO). Overall, onset features and hematologic biomarkers were found to be reliable information that can be easily obtained in clinical settings to aid in the differential diagnosis of unipolar and bipolar depression.

Izabela Guimarães Barbosa et al. [100] carried out a study aiming to identify clinical and immune predictors of cognitive performance in bipolar disorder (BD) patients. The study involved remitted BD patients (mean age ± standard error: 43.80 ± 10.87 years) and age-matched controls (mean age ± standard error: 43.52 ± 11.72 years). Participants underwent clinical questionnaires and cognitive assessments, and inflammatory plasma levels (including IL-2, IL-4, IL-6, IL-10, IFN-γ, TNFα, IL-17A, sTNFR1, and sTNFR2) were measured via enzyme-linked immunosorbent assay. A global cognitive performance index was generated from BAC-A scores. Multivariate analyses were used to compare cognitive and immune parameters between groups. Results indicated a positive correlation between education and MMSE scores with global cognitive performance, while IL-6 plasma levels were negatively correlated with cognitive performance.

Mu-Hong Chen [101] conducted a study involving 110 patients diagnosed with affective disorders (59 with bipolar I disorder and 51 with major depressive disorder) who had a Global Assessment of Functioning score of ≥61, along with 51 age- and sex-matched controls. The study defined a body mass index (BMI) of ≥25 kg/m² as indicating obesity or overweight. Proinflammatory cytokines, including interleukin-6, tumor necrosis factor (TNF)-α, and C-reactive protein (CRP), were measured, and cognitive function was evaluated using the Wisconsin Card Sorting Test (WCST) and go/no-go task. Findings revealed that patients with bipolar I disorder or major depressive disorder were more inclined to be obese or overweight, had elevated CRP and TNF-α levels, and showed greater executive dysfunction in the WCST compared to controls. The study concluded that proinflammatory cytokines, rather than obesity or overweight, play a crucial role in affecting cognitive function in these patients, although a strong association between proinflammatory cytokines and obesity or overweight was also noted.

Sara Poletti et al. [102] conducted a neuropsychological assessment involving seventy-six inpatients consecutively admitted with a depressive episode as part of bipolar disorder. The evaluation used the Brief Assessment of Cognition in Schizophrenia, and blood plasma levels of various cytokines, chemokines, and growth factors were analyzed. The study found that higher levels of IL-1β, IL-6, CCL2, CCL4, CCL5, CXCL10, and bFGF were linked to a higher likelihood of poor cognitive performance, suggesting that a low-grade inflammatory state might contribute to the neurocognitive deficits observed in these depressed patients.

Linn Sofie Sæther et al. [103] sought to investigate the covariance patterns between inflammatory and immune-related markers and cognitive domains in individuals with severe mental illness (SMI). The study involved participants who met the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV criteria for schizophrenia or bipolar disorder spectrum disorders. The researchers recruited a total of 1402 participants, including 343 with schizophrenia, 289 with bipolar disorder spectrum disorders, and 770 healthy controls. Data collection occurred from outpatient and inpatient psychiatric units in the Oslo area between 2004 and 2018. The study identified shared covariance between verbal learning and psychomotor processing speed and markers of innate immune activation, such as IL-18, IL-18BP, beta-defensin 2 (BD2), and VCAM-1. They found that poorer verbal learning and slower psychomotor processing speed were linked to higher levels of IL-18 system cytokines and BD2, indicating increased innate immune activation. This pattern was more pronounced in individuals with SMI compared to healthy controls. Hierarchical clustering of covariance patterns, identified through canonical correlation analysis, revealed a subgroup with high cognition and low immune dysregulation, primarily composed of healthy controls (24% schizophrenia, 45% bipolar disorder, 74% healthy controls), and a subgroup with low cognition and high immune dysregulation,

predominantly consisting of SMI patients (76% schizophrenia, 55% bipolar disorder, 26% healthy controls).

MATERIALS AND METHODS

SOURCE OF DATA: A study was conducted on patients diagnosed with bipolar disorder presenting to DMC &H Ludhiana.

METHOD OF COLLECTION OF DATA

SAMPLE COLLECTION- The study included 100 patients in the age group of 18-65 years presenting with bipolar affective disorder to the Department of Psychiatry in DMC&H Hospital, Ludhiana, and 30 healthy donors in the age group of 18-65 years.

INCLUSION CRITERIA:

1. The patients with a diagnosis of bipolar affective disorder according to DSM-5 criteria presenting to DMC&H, Ludhiana.

2. Age between 18 years to 65 years.

3. Patients who gave consent for participation in the study.

FOR CONTROLS:

1. The patient not having any history of bipolar disorder or any other psychiatric illness.

2. Age group between 18 years to 65 years.

3. Individuals who gave consent for the study

EXCLUSION CRITERIA:

1. Any other major psychiatric disorder in patients except for bipolar affective disorder

2. History of any known uncontrolled medical comorbidity.

3. Patient receiving any anti-inflammatory treatment (non-steroidal anti-inflammatory drug, corticosteroid, or other anti-inflammatory drug)

4. Female patients currently having pregnancy and lactation.

5. Patients with intake of antibiotics 2 weeks before the study or during the study.

6. Patients who have not given consent for the study.

FOR CONTROLS:

1. Any current psychiatric or neurological disorder.
2. Ongoing treatment with psychotropic medications.
3. A past history of bipolar disorder, schizophrenia, recurrent depression, or other psychiatric conditions.
4. Having a first-degree relative diagnosed with schizophrenia or bipolar disorder.

STUDY DESIGN: The study involved 100 consecutive patients aged 18-65 years diagnosed with bipolar disorder, presenting to the Department of Psychiatry at DMC&H Ludhiana, and 30 healthy controls aged 18-65 years. To qualify, patients needed to meet the inclusion criteria and provide written informed consent before being enrolled. Cognitive functions were evaluated using neuropsychological assessment tests. Blood tests were conducted to measure absolute counts of neutrophils, lymphocytes, monocytes, and platelets, and the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR) were calculated accordingly. Cognitive and biochemical markers were assessed on day 1, after 3 weeks, and again after 16 weeks.

TOOLS:

PGI MEMORY SCALE: The PGI Memory Scale (PGIMS) was incorporated into the Battery of Brain Dysfunction. The PGIMS offers a comprehensive yet straightforward scale for measuring both verbal and nonverbal memories based on neurological theory. It evaluates very short-term, short-term, and long-term memory, supported by experimental evidence, and remote, recent, and immediate memory, derived from clinical practice. The scale consists of 10 subtests:

1. Remote memory
2. Recent memory
3. Mental balance
4. Attention
5. Delayed recall
6. Immediate recall (sequential reproduction of sentences)
7. Retention for similar pairs
8. Retention for dissimilar pairs
9. Visual retention
10. Recognition

Psychometric Properties:

- Subtest 1: Scores 1 point for each correct answer (maximum score: 7).
- Subtest 2: Scores 1 point for each correct answer (maximum score: 5).

- Subtest 3: For the first two questions, score 3 points if all answers are correct within 15 seconds, 2 points if it takes longer than 15 seconds, and 1 point if there is one mistake or omission (0 points for two or more mistakes). For the last question, score 3 points if all answers are correct within 30 seconds, 2 points if it takes longer than 30 seconds, 1 point if there is one mistake, and 0 points for two or more mistakes (maximum score: 9).

- Subtest 4: For the first question, 3-4 digits score 1 point, 5-6 digits score 2 points (1 point for a mistake), and 7-8 digits score 3 points (2 points for one mistake and 0 points for more than two mistakes) (maximum score: 12).

- Subtest 5: one point for each correctly recalled word, up to a maximum of 10 points.

- Subtest 6: one point for accurately reproducing each clause, with a maximum possible score of 12.

- Subtest 7: One point is allocated for each correct response in recalling an associated word from a pair, with a total of 5 points.

- Subtest 8: Score one point for each pair correctly reproduced in each trial. The total score is the sum of the scores from three trials, up to 15 points.

- Subtest 9: Points are given for accurately reproducing each type of geometric figure in the correct sequence and quantity; cards 1 to 3 earn 2 points each, card 4 earns 3 points, and card 5 earns 4 points, for a total of 13 points.

- Subtest 10: Each object that is correctly recognized and named scores one point. Points are deducted for each object incorrectly identified, with a total potential score of 10.

- TRAIL MAKING TEST: The Trail Making Test (TMT) is a timed neuropsychological assessment that measures visual scanning and working memory. It consists of two parts: TMT A (rote memory) and TMT B (executive functioning). In each part, participants draw a line connecting 24 consecutive circles arranged randomly on a page. TMT A involves connecting numbers, while TMT B alternates between numbers and letters, requiring the participant to switch between them in sequential order. The test is scored based on the time taken to complete it, including any corrections prompted by the examiner. If the participant cannot complete the test within 5 minutes, it is discontinued. An average score for TMT A is 29 seconds, with scores greater than 78 seconds considered deficient. For TMT B, an average score is 75 seconds, with scores exceeding 273 seconds deemed deficient. Normative data has been established based on age and education.

3. DIGIT SYMBOL SUBSTITUTION TEST: The Digit Symbol Substitution Test (DSST) assesses response speed, sustained attention, visuospatial skills, and set-shifting. It is a component of the Wechsler Adult Intelligence Scale, a highly utilized measure of intelligence. During the DSST, participants are required to correctly fill in a series of symbols according to a provided code within 90 seconds. In this test, a higher score indicates better performance.

4. **HAEMATOLOGICAL INDICES**

PARAMETER	**NORMAL VALUE**
1. Absolute neutrophil count:	2 – 7 $X10^3$/ Ul
2. Absolute lymphocyte count:	0.8 – 4 $X10^3$/ Ul
3. Absolute monocyte count:	0.12 – 1.2 $X10^3$/ Ul
4. Platelet count:	150-400 X 10^3/ ul

The reference ratio value will be calculated normal study group.

Statistical Analysis

Data is presented as ranges, mean ± standard deviation (± SD), median, frequencies (number of cases), and relative frequencies (percentages), as appropriate. The Kolmogorov-Smirnov test was employed to assess the normality of data distribution. Quantitative variables were compared between study groups using the Student t-test for parametric data and the Mann-Whitney U test for non-parametric data. Categorical data comparisons were performed using the Chi-square ($\chi 2$) test, with the Fisher exact test applied when expected frequencies were less than 5. Spearman's rho correlation analysis was used to assess relationships between variables. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were conducted using the SPSS version 21 software (SPSS Inc., Chicago, IL, USA) for Microsoft Windows.

OBSERVATION AND RESULTS

The study included 100 patients with bipolar disorder and 30 healthy controls, enrolled at DMC&H, Ludhiana. Participants were followed up at week 1, week 3, and week 16. The collected data was tabulated and analyzed, yielding the following results.

AGE GROUP	CASES		CONTROL		TOTAL	Chi-square value	p-value
	No	%age	No	%age			
< 30	19	19.0	7	23.3	26	4.782	0.188
31-40	28	28.0	6	20.0	34		
41-50	23	23.0	12	40.0	35		
> 50	30	30.0	5	16.7	35		
Total	100	100.0	30	100.0	130		

TABLE NO. 1 DISTRIBUTION OF SUBJECTS ACCORDING TO AGE

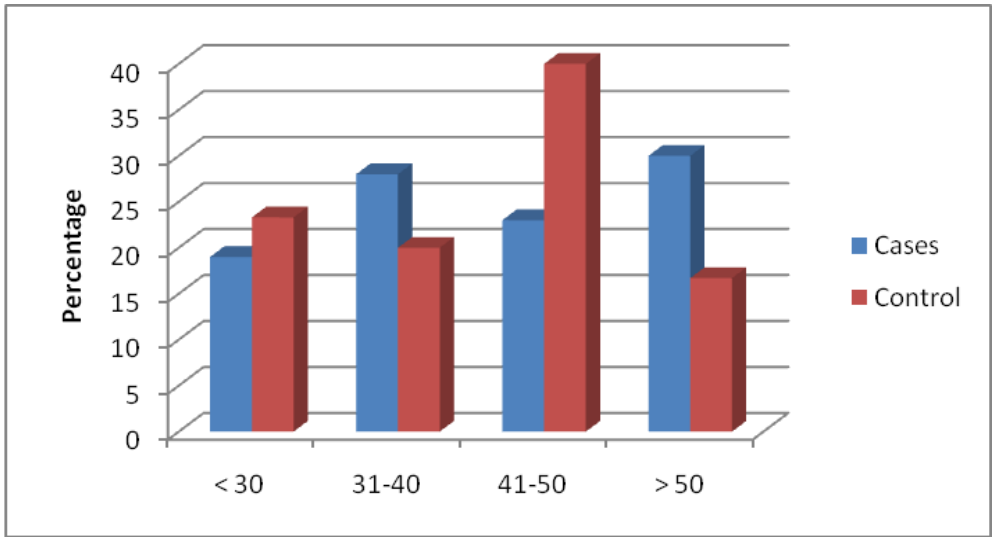

FIGURE NO. 1 DISTRIBUTION OF SUBJECTS ACCORDING TO AGE

; Shows thatthe majority of cases were in the > 50 years age group and the majority of control subjects were in the 41-50 years age group

GENDER	CASES		CONTROL		TOTAL	Chi-square value	p-value
	NO	%	NO	%			
FEMALE	31	31.0	10	33.3	41	0.058	0.809
MALE	69	69.0	20	66.7	89		
TOTAL	100	100.0	30	100.0	130		

TABLE NO. 2 DISTRIBUTION OF SUBJECTS ACCORDING TO GENDER

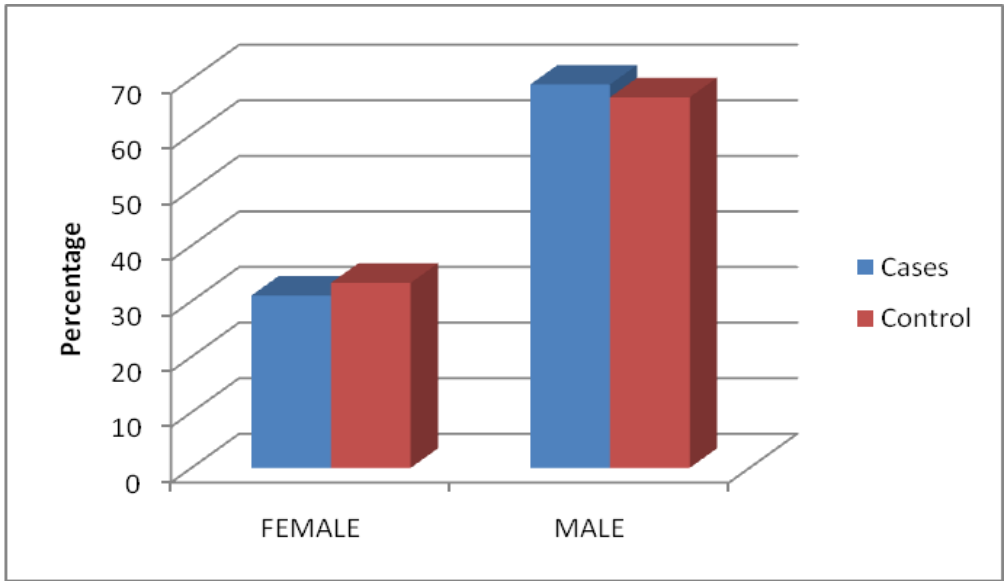

FIGURE NO. 2 DISTRIBUTION OFSUBJECTS ACCORDING TO GENDER

; In both the cases and control groups, the majority gender was male.

MARITAL STATUS	CASES		CONTROL		TOTAL	Chi-square value	p-value
	NO	%AGE	NO.	%AGE			
MARRIED	82	82.0	24	80.0	106	0.061	0.804
UNMARRIED	18	18.0	6	20.0	24		
TOTAL	100	100.0	30	100.0	130		

TABLE NO. 3 DISTRIBUTION OF SUBJECTS ACCORDING TO MARITAL STATUS

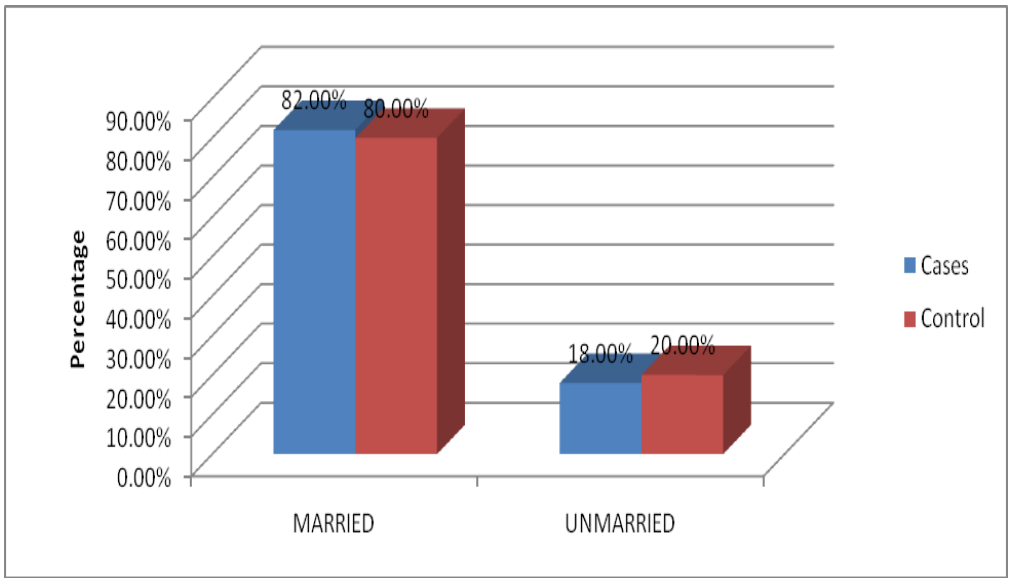

FIGURE NO. 3 DISTRIBUTION OF SUBJECTS ACCORDING TO MARITAL STATUS

; Shows that a majority of both the case group (82%) and the control group (80%) were married.

EDUCATION	CASES		CONTROL		TOTAL	Chi-square value	p-value
	NO.	%AGE	NO.	%AGE			
DIPLOMA	1	1.0	0	0.0	1	8.66	0.194
GRADUATION	33	33.0	9	30.0	42		
HIGHER SECONDARY	16	16.0	10	33.3	26		
MATRICULATION	28	28.0	4	13.3	32		
MIDDLE SCHOOL	5	5.0	0	0	5		
POST-GRADUATE	9	9.0	5	16.7	14		
PRIMARY	8	8.0	2	6.7	10		
TOTAL	100	100.0	30	100.0	130		

TABLE NO. 4 DISTRIBUTION OF SUBJECTS ACCORDING TO EDUCATION

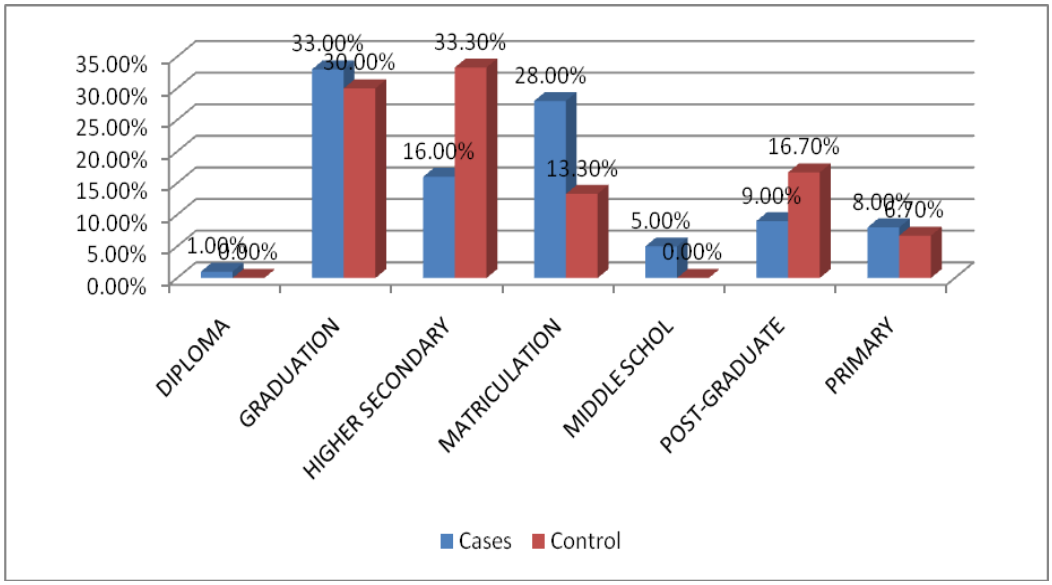

FIGURE NO. 4 DISTRIBUTION OF SUBJECTS ACCORDING TO EDUCATION

; Shows Graduation was the most common level of education among cases (33%) and controls (30%).

OCCUPATION	CASES		CONTROL		TOTAL	Chi-square value	p-value
	NO.	%AGE	NO.	%AGE			
PROFESSIONAL	11	11.0	6	20.0	17	6.49	0.261
SEMIPROFESSIONAL	11	11.0	4	13.3	15		
SEMISKILLED	27	27.0	6	20.0	33		
SKILLED WORKER	3	3.0	3	10.0	6		
UNEMPLOYED	45	45.0	9	30.0	54		
UNSKILLED	3	3.0	2	6.7	5		
TOTAL	100	100	30	100.0	130		

TABLE NO. 5 DISTRIBUTION OF SUBJECTS ACCORDING TO OCCUPATION

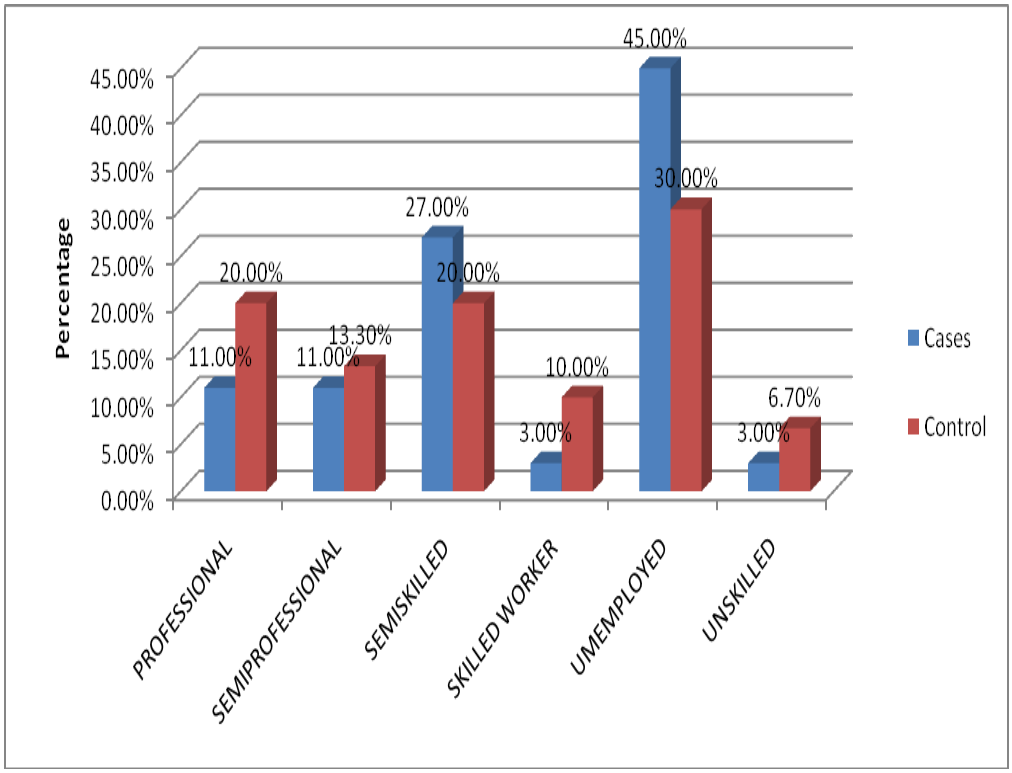

FIGURE NO. 5 DISTRIBUTION OF SUBJECTS ACCORDING TO OCCUPATION

; Shows that the largest group within the cases and controls was unemployed individuals, comprising 45%, compared to 30% in the control group.

FAMILY TYPE	CASES		CONTROL		TOTAL	Chi-square value	p-value
	NO.	%AGE	NO.	%AGE			
JOINT	23	23	7	23.3	30		
NUCLEAR	77	77	23	76.7	100	0.001	0.97
TOTAL	100	100	30	100	130		

TABLE NO. 6 DISTRIBUTION OF SUBJECTS ACCORDING TO FAMILY TYPE

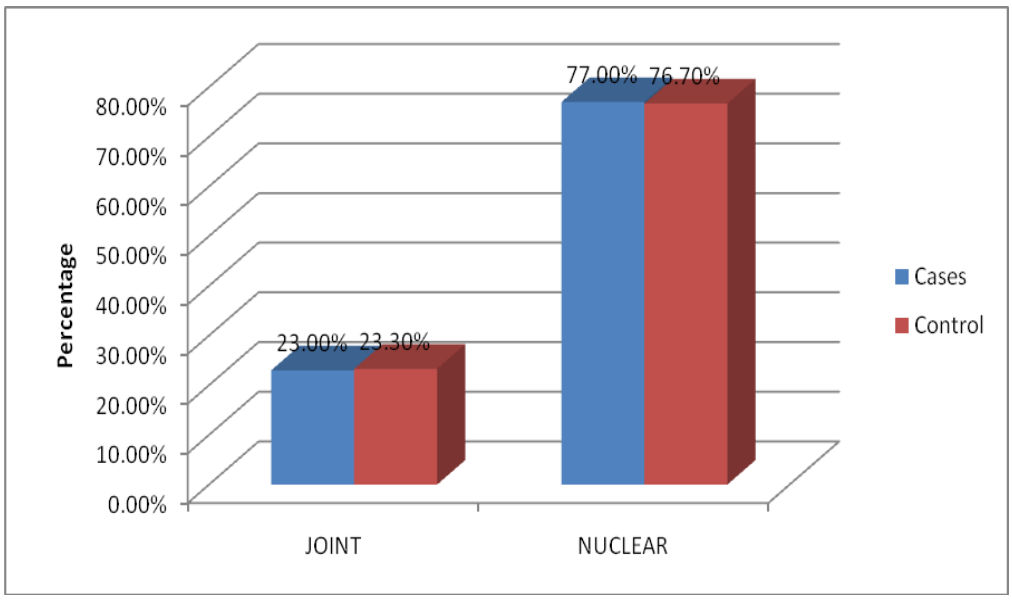

FIGURE NO. 6 DISTRIBUTION OF SUBJECTS ACCORDING TO FAMILY TYPE

; Shows that the majority of cases (77%) and controls (76.7%) were from nuclear families.

RELIGION	CASES		CONTROL		TOTAL	Chi-square value	p-value
	NO.	%AGE	NO.	%AGE			
CHRISTIAN	1	1.0	1	3.3	2	5.563	0.062
HINDU	42	42.0	19	63.3	61		
SIKH	57	57.0	10	33.3	67		
TOTAL	100	100.0	30	100.0	130		

TABLE NO. 7 DISTRIBUTION OF SUBJECTS ACCORDING TO RELIGION

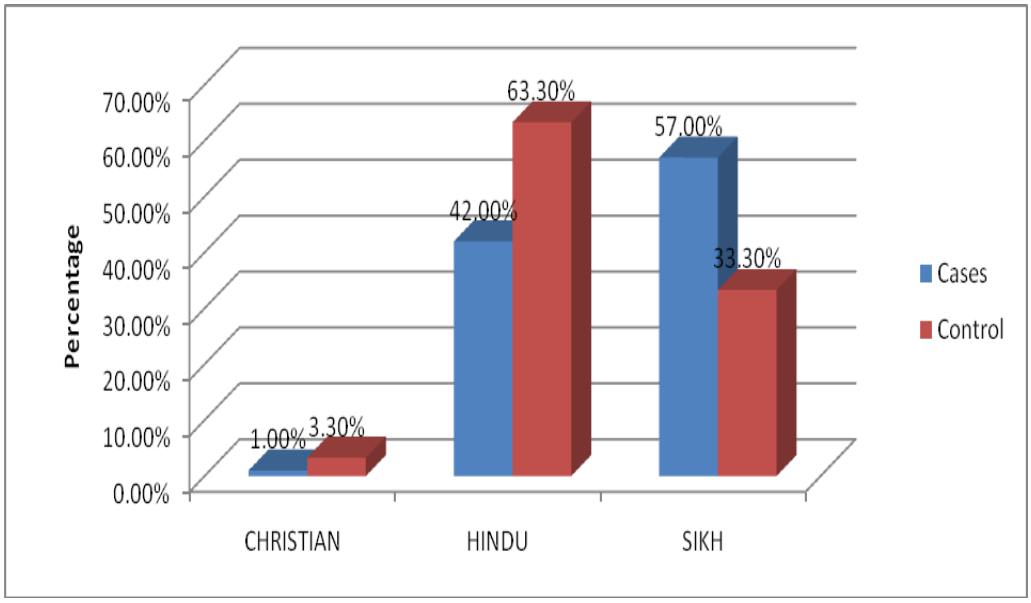

FIGURE NO. 7 DISTRIBUTION OF SUBJECTS ACCORDING TO RELIGION

; Shows that the majority of cases and controls belonged to Sikh and Hindu religions respectively.

RESIDENCE	CASES		CONTROL		TOTAL	Chi-square value	p-value
	NO.	%AGE	NO.	%AGE			
RURAL	43	43.0	13	43.3	56	0.001	0.974
URBAN	57	57.0	17	56.7	74		
TOTAL	100	100.0	30	100.0	130		

TABLE NO. 8 DISTRIBUTION OF SUBJECTS ACCORDING TO RESIDENTIAL OCCUPANCY

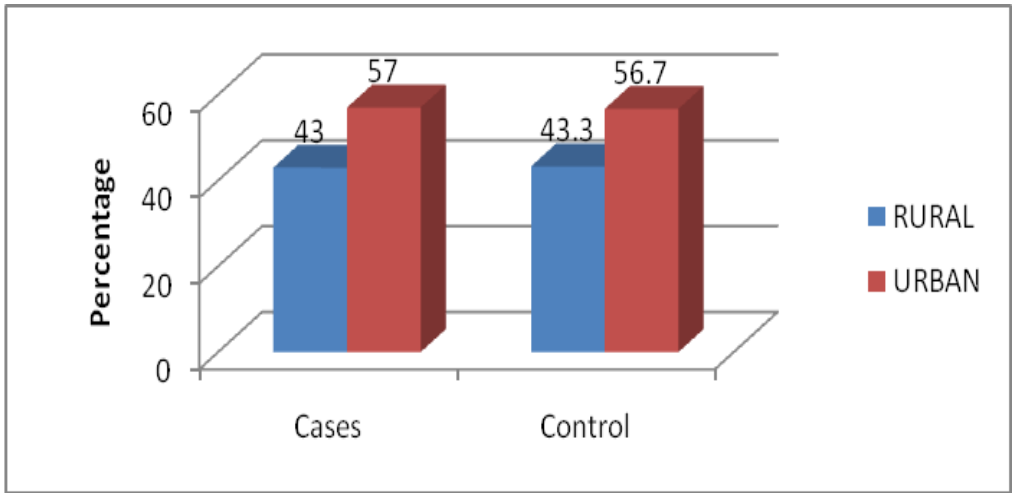

FIGURE NO. 8 DISTRIBUTION OF SUBJECTS ACCORDING TO RESIDENTIAL OCCUPANCY

; shows that the majority of cases (57%) and controls (56.7%) resided in urban areas.

FAMILY HISTORY OF BIPOLAR DISORDER	CASES	
	NO.	%AGE
ABSENT	79	79
PRESENT	21	21
TOTAL	100	100

TABLE NO. 9 FAMILY HISTORY OF BIPOLAR DISORDER IN CASES.

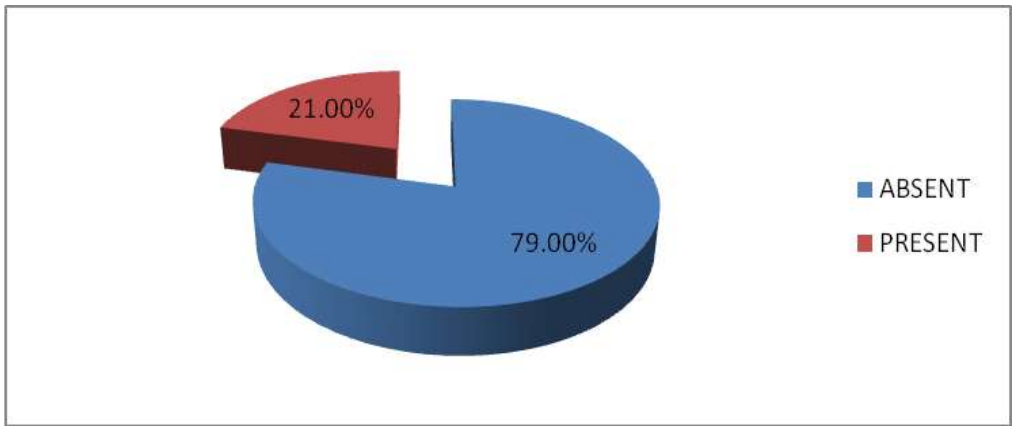

FIGURE NO. 9 FAMILY HISTORY OF BIPOLAR DISORDER IN CASES

; indicates that the majority of the cases (79%) did not have a family history of bipolar disorder

MOOD STABILIZERS	Cases	
	No.	%age
LITHIUM	56	56
SODIUM VALPROATE	44	44
TOTAL	100	100

TABLE NO. 10 DISTRIBUTION ACCORDING TO TYPE OF MOOD STABILIZER IN CASES

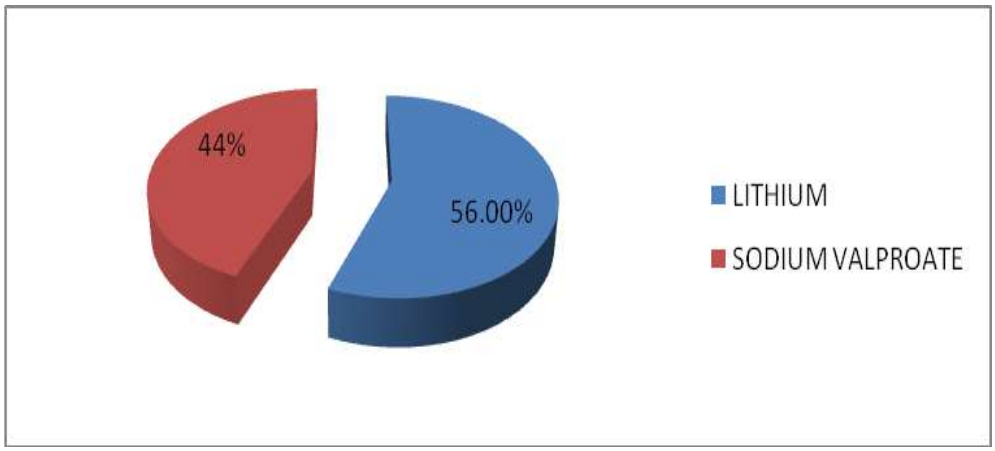

FIGURE NO. 10 DISTRIBUTION ACCORDING TO TYPE OF MOOD STABILIZER IN CASES

; Indicates that the majority of cases (56%) were on lithium.

	CASES		CONTROL		Z	p-value
	Mean	SD	Mean	SD		
AGE	43.00	13.00	41.00	10.57	0.789	0.443
INCOME	56096.00	65126.96	54966.33	44949.12	-0.589	0.556

TABLE NO 11. MEAN AGE AND INCOME OF SUBJECTS

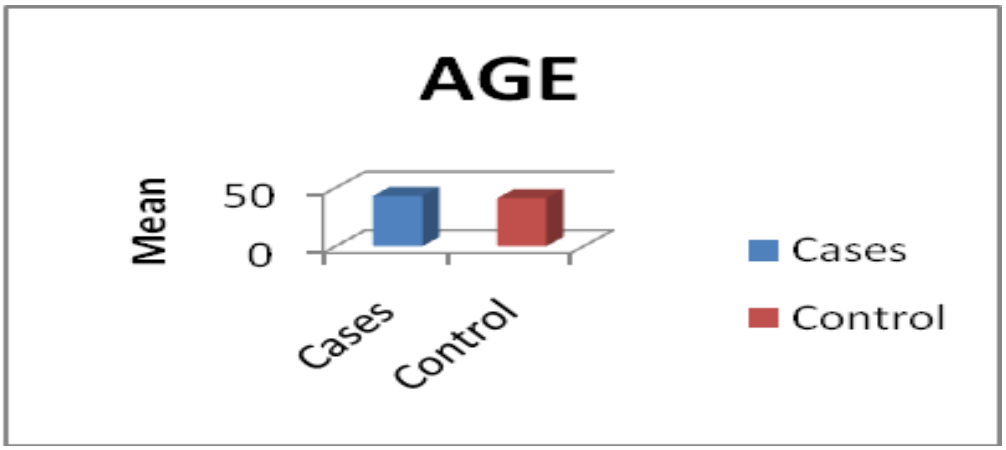

FIGURE NO.11 (A) MEAN AGE OF THE SUBJECTS

; The mean age for cases was 43 years (SD: 13), whereas for controls, it was 41 years (SD: 10.57).

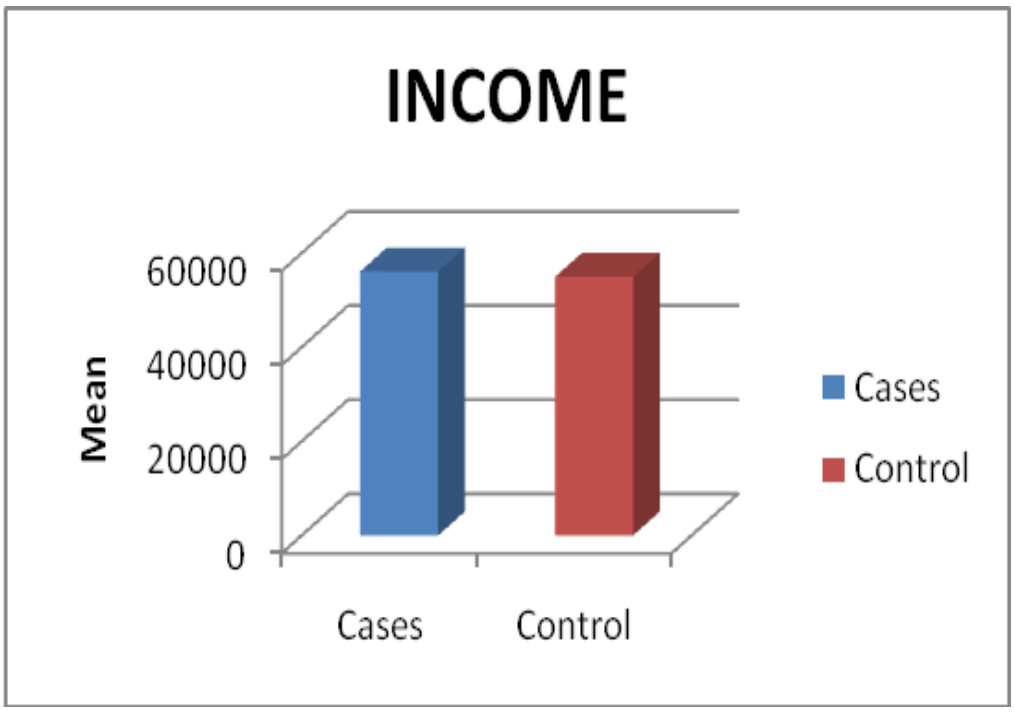

FIGURE NO.11 (B) MEAN INCOME OF THE SUBJECTS

; Shows the mean income for cases was Rs. 56,096 (SD: 65,126.96), for controls It was Rs. 54,966.33 (SD: 44,949.12).

DURATION OF ILLNESS (YEARS)	CASES	
	NO.	%AGE
< 5	39	39
5-10.0	21	21
> 10	40	40
Total	100	100
MEAN DURATION OF ILLNESS (YEARS)	12.6	11.7

TABLE No. 12 DISTRIBUTION OF CASES ACCORDING TO DURATION OF ILLNESS

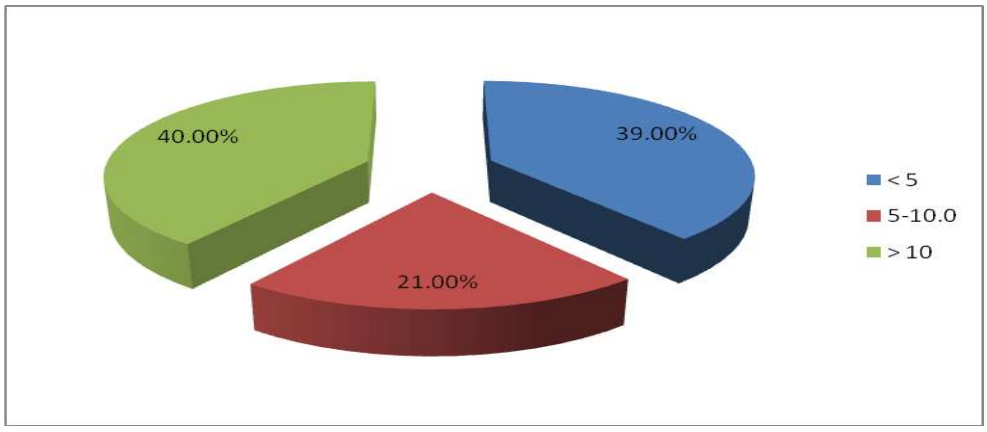

FIGURE NO. 12 DISTRIBUTION OF CASES ACCORDING TO DURATION OF ILLNESS

; Majority of the cases (40%) had duration of illness more than 10 years.

	CASES		CONTROL		Z	p-value
	Mean	SD	Mean	SD		
REMOTE MEMORY	5.67	0.67	5.70	0.47	-0.426	0.670
RECENT MEMORY	4.74	0.48	5.00	0.37	-2.630	0.009
MENTAL BALANCE	7.59	1.38	7.63	0.85	-0.089	0.929
ATTENTION AND CONCENTRATION	9.20	1.69	12.03	1.61	-6.331	0.001
DELAYED RECALL	8.64	1.43	9.63	0.49	-3.415	0.001
IMMEDIATE RECALL	10.96	1.14	11.77	0.63	-3.944	0.001
RETENTION FOR SIMILAR PAIRS	4.46	0.82	4.50	0.51	-0.619	0.536
RETENTION FOR DISSIMILAR PAIRS	10.82	3.00	11.03	1.52	-0.414	0.679
VISUAL RETENTION	10.51	2.06	12.07	0.94	-4.327	0.001
RECOGNITION	8.64	1.11	9.57	0.63	-4.382	0.001

TABLE NO. 13 COMPARISON OF COGNITIVE FUNCTIONS OF SUBJECTS AT WEEK 1

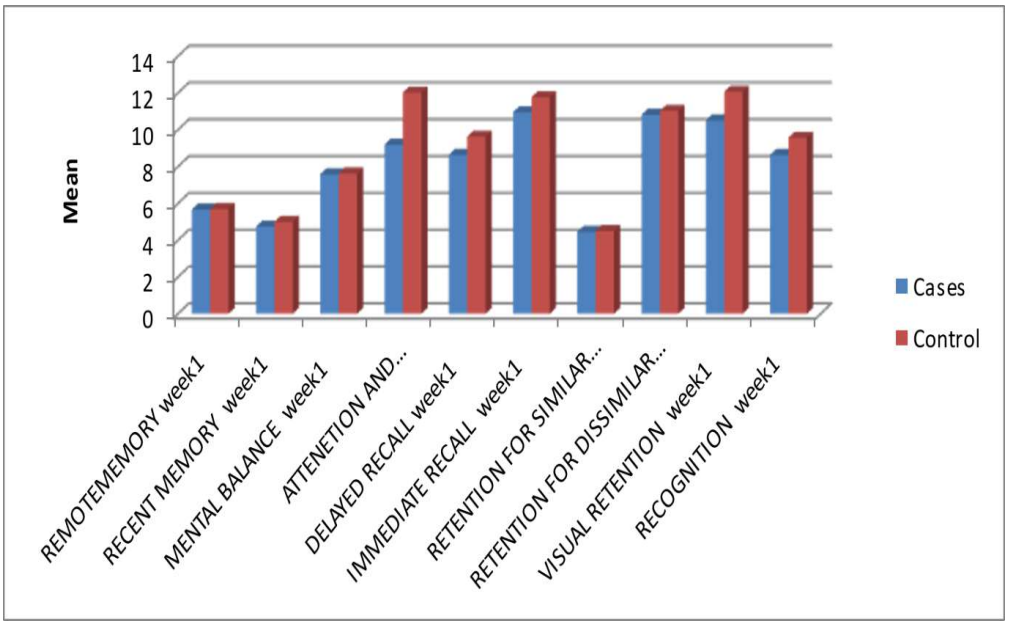

FIGURE NO. 13 COMPARISON OF COGNITIVE FUNCTIONS OF SUBJECTS AT WEEK 1

; Cases showed significantly lower mean scores in recent memory, attention andconcentration, delayed recall, immediate recall, visual retention, and recognition than controls at week 1

	CASES		CONTROL		Z	p-value
	Mean	SD	Mean	SD		
REMOTE MEMORY	5.66	0.68	5.70	0.47	-0.021	0.983
RECENT MEMORY	4.72	0.49	4.93	0.25	-2.331	0.020
MENTAL BALANCE	7.17	1.41	7.43	0.94	-0.451	0.652
ATTENTIONAND CONCENTRATION	8.79	1.76	11.97	1.47	-6.753	0.001
DELAYED RECALL	8.30	1.54	9.70	0.47	-5.108	0.001
IMMEDIATE RECALL	10.89	1.29	11.93	0.74	-4.387	0.001
RETENTION FOR SIMILAR PAIRS	4.35	0.88	4.50	0.51	-0.139	0.889
RETENTION FOR DISSIMILAR PAIRS	11.06	2.98	11.30	1.97	-0.318	0.750
VISUAL RETENTION	10.75	2.00	12.27	0.74	-3.785	0.001
RECOGNITION	8.67	1.19	9.70	0.47	-4.656	0.001

TABLE NO. 14 COMPARISON OF COGNITIVE FUNCTIONS OF SUBJECTS AT WEEK 3

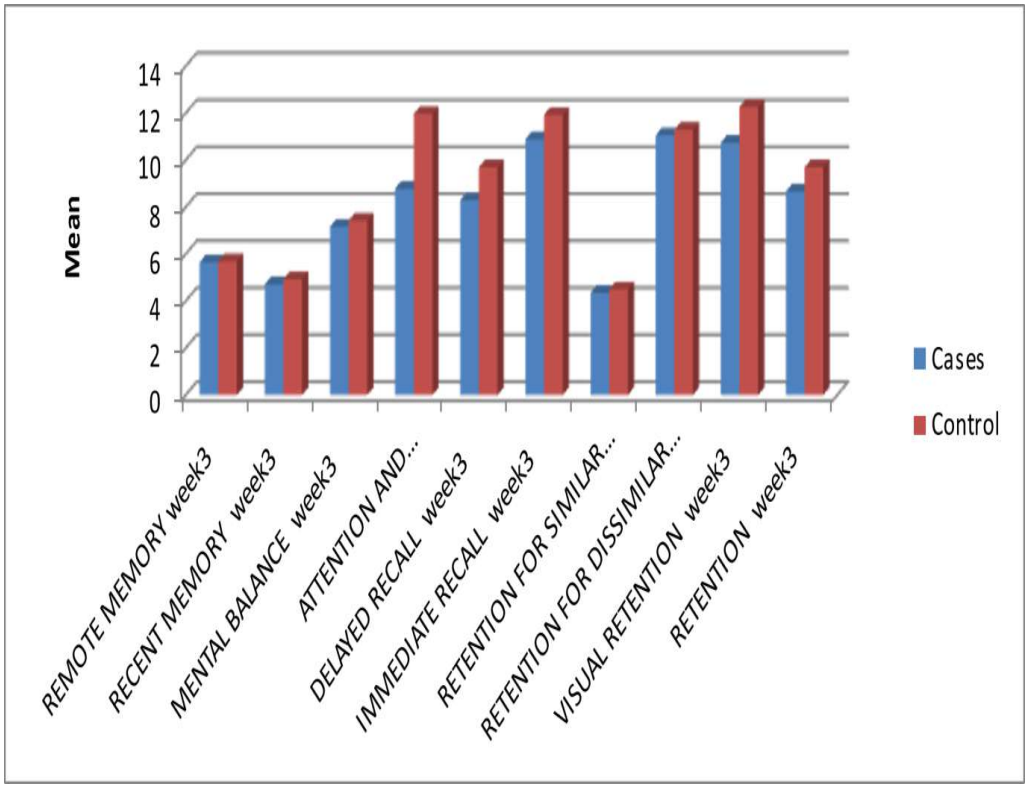

FIGURE NO. 14 COMPARISON OF COGNITIVE FUNCTIONS OF SUBJECTS AT WEEK 3

; Cases showed significantly lower mean scores in recent memory, attention and concentration, delayed recall, immediate recall, visual retention, and recognition than controls at week 3

	CASES		CONTROL		Z	p-value
	Mean	SD	Mean	SD		
REMOTE MEMORY	5.57	0.71	5.70	0.47	-0.478	0.633
RECENT MEMORY	4.76	0.59	4.93	0.25	-2.119	0.034
MENTAL BALANCE	6.88	1.44	7.43	0.94	-1.449	0.147
ATTENTION AND CONCENTRATION	8.38	1.33	12.07	1.26	-7.955	0.001
DELAYED RECALL	7.93	1.63	9.83	0.38	-6.709	0.001
IMMEDIATE RECALL	10.55	1.28	12.13	0.57	-6.348	0.001
RETENTION FOR SIMILAR PAIRS	4.35	0.70	4.47	0.51	-0.510	0.610
RETENTION FOR DISSIMILAR PAIRS	10.80	3.50	11.13	1.81	-0.824	0.410
VISUAL RETENTION	10.07	2.39	12.23	0.68	-5.592	0.001
RECOGNITION	8.57	1.22	9.87	0.35	-5.672	0.001

TABLE NO. 15 COMPARISON OF COGNITIVE FUNCTIONS OF SUBJECTS AT WEEK 16

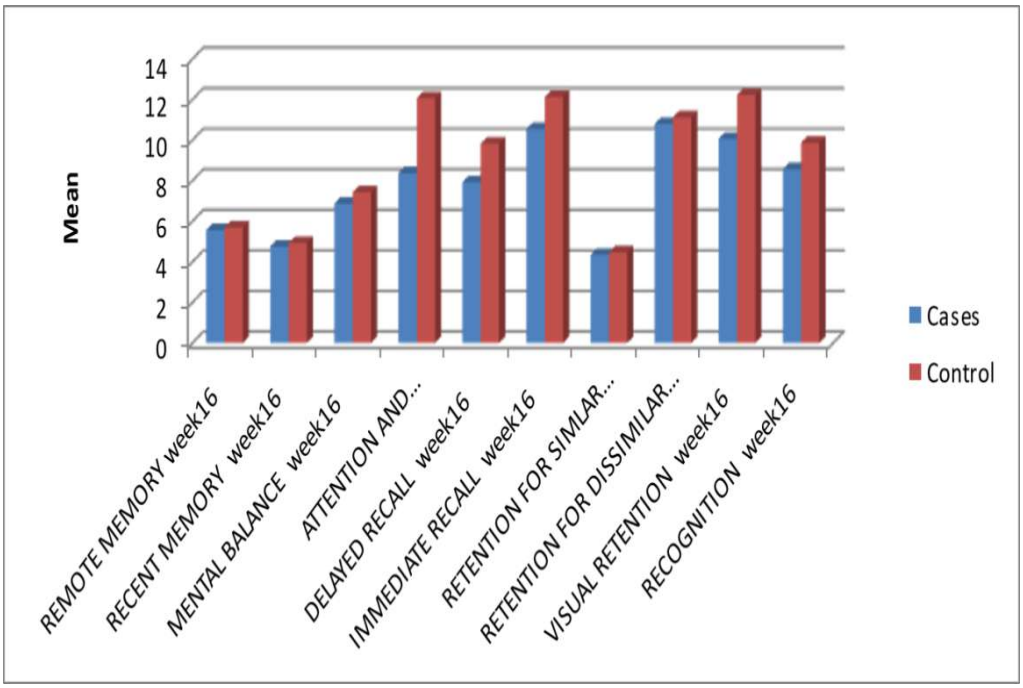

FIGURE NO. 15 COMPARISON OF COGNITIVE FUNCTIONS OF SUBJECTS AT WEEK 16

; Cases showed significantly lower mean scores in recent memory, attention and concentration, delayed recall, immediate recall, visual retention, and recognition than controls at week 16

	CASES		CONTROL		Z	p-value
	Mean	SD	Mean	SD		
TOTAL SCORE OF MEMORY WEEK 1	82.08	11.47	92.90	3.16	-4.463	0.001
TOTAL SCORE OF MEMORY WEEK 3	81.59	12.07	93.90	3.03	-4.894	0.001
TOTAL SCORE OF MEMORY WEEK 16	79.18	12.37	94.10	3.04	-7.201	0.001
Δ TOTAL SCORE OF MEMORY WEEK 3	0.49	2.42	-1.00	1.80	-3.436	0.001
Δ TOTAL SCORE OF MEMORY WEEK 16	2.90	4.66	-1.20	3.39	-5.497	0.001

TABLE NO. 16 COMPARISON OF TOTAL SCORE OF MEMORY OF SUBJECTS OF AT WEEKS 1,3 AND 16, AND THE CHANGE IN TOTAL MEMORY SCORE FROM BASELINE TO WEEKS 3 AND 16

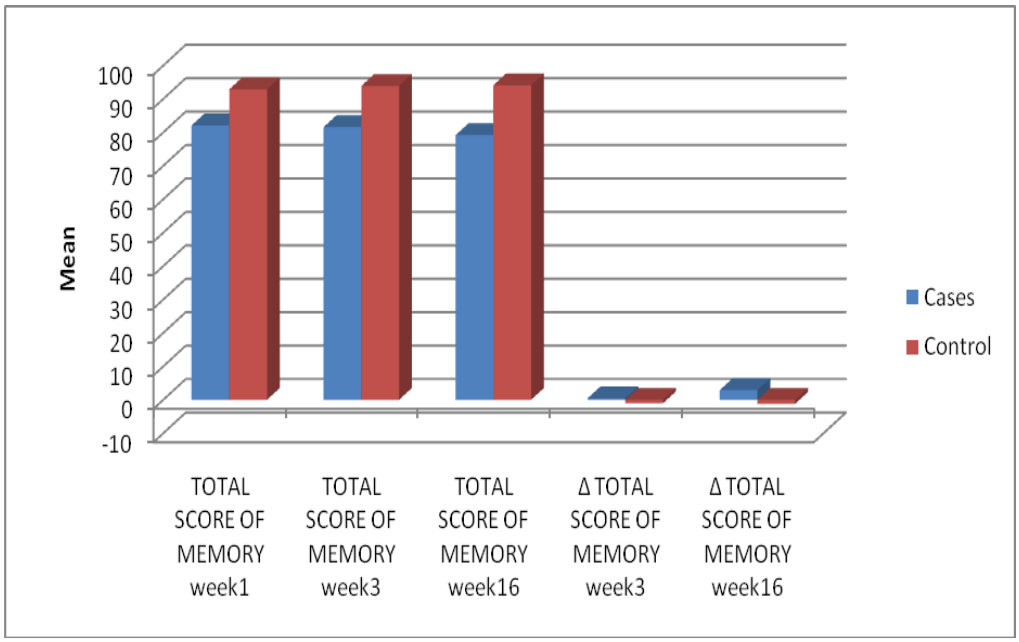

FIGURE NO. 16 COMPARISON OF THE TOTAL SCORE OF MEMORY OF SUBJECTS AT WEEKS 1,3 AND 16, AND THE CHANGE IN TOTAL SCORE OF MEMORY FROM BASELINE TO WEEKS 3 AND 16

; Shows that case consistently had significantly lower total score of memory than controls at weeks 1, 3, and 16. Changes in the total score of memory over time showed significant differences between cases and controls, cases experienced a greater decline in total score of memory.

	CASES		CONTROL		Z	p-value
	Mean	SD	Mean	SD		
DSST WEEK 1	33.18	12.17	79.60	9.51	-8.232	0.001
DSST WEEK 3	31.84	12.19	80.10	9.22	-8.251	0.001
DSST WEEK 16	32.81	14.44	80.17	9.17	-8.258	0.001
Δ DSST WEEK 3	1.34	2.66	-0.50	0.97	-3.989	0.001
Δ DSST WEEK 16	0.37	7.65	-0.57	1.30	-1.674	0.094

TABLE NO. 17. COMPARISON OF DIGIT SYMBOL SUBSTITUTION TEST (DSST) SCORES OF SUBJECTS AT WEEKS 1,3 AND 16 AND CHANGE IN DSST FROM BASELINE TO WEEKS 3 AND 16.

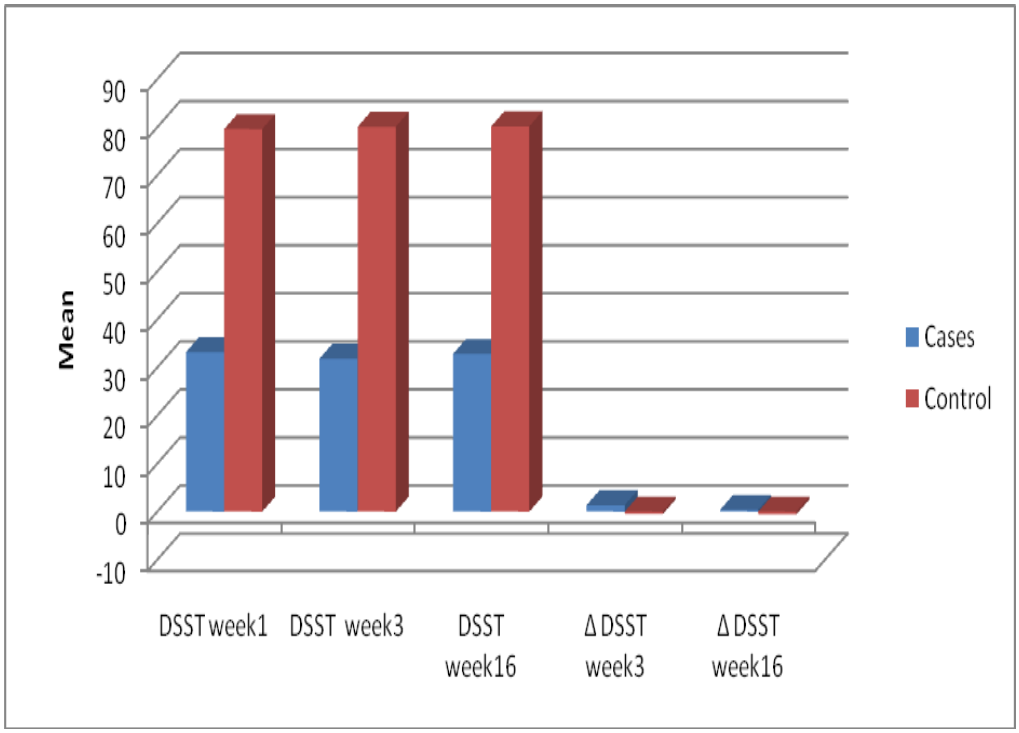

FIGURE NO. 17 COMPARISON OF DIGIT SYMBOL SUBSTITUTION TEST (DSST) SCORES OF SUBJECTS AT WEEKS 1,3 AND 16 AND CHANGE IN DSST FROM BASELINE TO WEEKS 3 AND 16.

; Shows that cases had significantly lower DSST scores at week 1, week 3, and week 16. The mean change from baseline to 3 weeks between cases and controls shows a significant difference indicating a decline in processing speed and visual motor integration skills in cases.

	CASES		CONTROL		Z	p-value
	Mean	SD	Mean	SD		
TMT A WEEK 1	75.04	56.08	31.03	7.29	4.276	0.000
TMT A WEEK 3	82.62	75.43	30.67	6.48	3.758	0.000
TMT A WEEK 16	84.15	92.30	30.47	6.85	3.174	0.002
ΔTMT A 3 WEEK	-7.58	33.04	0.37	1.61	-1.313	0.191
Δ TMT AWEEK 16	-9.11	49.91	0.57	1.52	-1.059	0.292

TABLE NO.18 COMPARISON OF TRAIL MAKING TEST A (TMT A) DURATION OF SUBJECTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

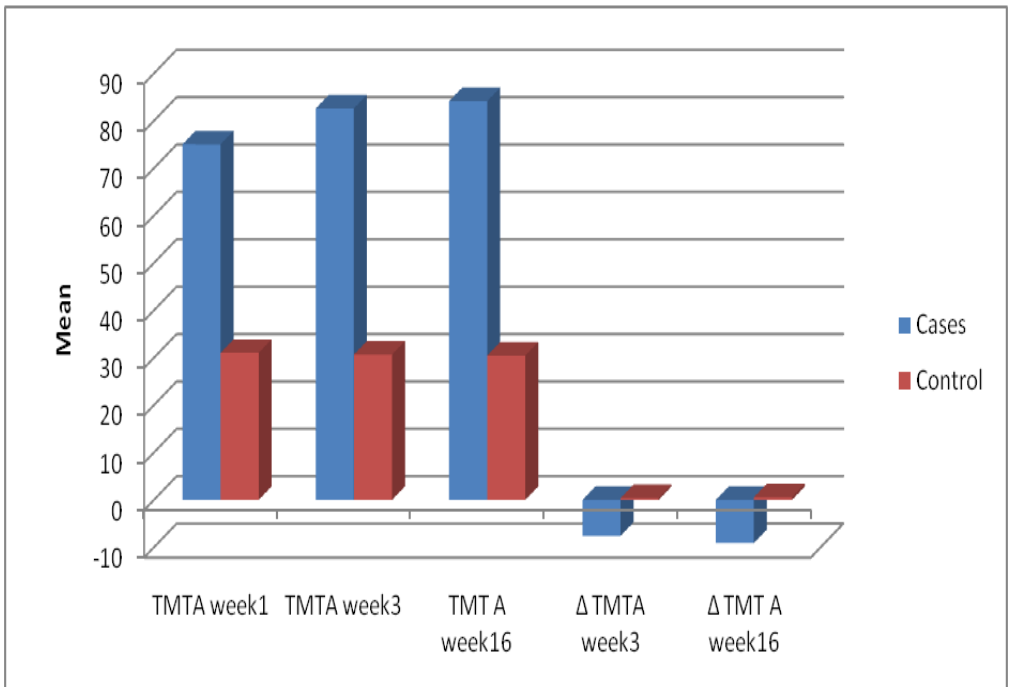

FIGURE NO. 18 COMPARISON OF TRAIL MAKING TEST A (TMT A) DURATION OF SUBJECTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

; Indicates that cases had significantly higher Trail Making Test A (TMT A) duration compared to controls at weeks 1, 3, and 16. This suggests worse executive functions in cases at each time point.

	CASES		CONTROL		Z	p-value
	Mean	SD	Mean	SD		
TMT B WEEK 1	125.88	86.28	63.87	25.94	-5.566	0.001
TMT B WEEK 3	113.77	74.66	63.13	24.36	-4.827	0.001
TMT B WEEK 16	108.19	69.34	63.10	23.83	-4.438	0.001
Δ TMT B WEEK 3	12.11	28.05	0.73	3.68	-3.923	0.001
Δ TMT B WEEK 16	17.69	34.02	0.77	3.49	-4.724	0.001

TABLE NO. 19 COMPARISON OF TRAIL MAKING TEST B (TMT B) DURATION OF SUBJECTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

.

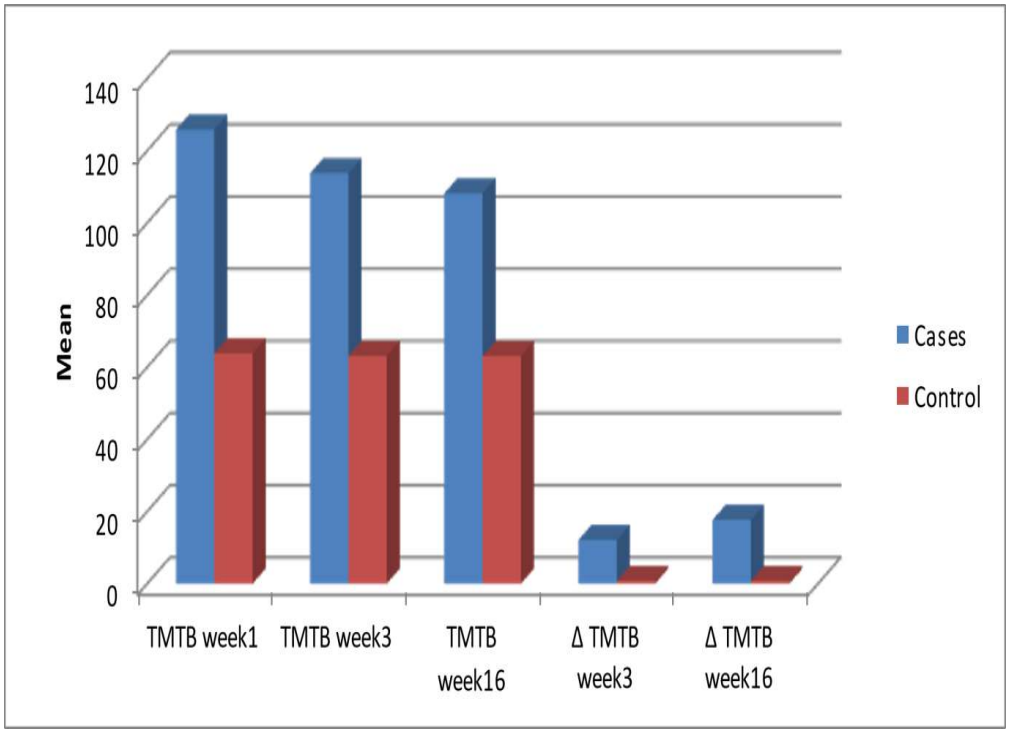

FIGURE NO. 19 COMPARISON OF TRAIL MAKING TEST B (TMT B) DURATION OF SUBJECTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

; Shows that the cases had more difficulty with cognitive flexibility, executive function, processing speed, and visual attention at each time point (weeks 1, 3, and 16). The significant differences in score changes from baseline to weeks 3 and 16 weeks suggest that the cases experienced more substantial deterioration in these cognitive functions over time compared to the controls.

	CASES		CONTROL		Z	p-value
	Mean	SD	Mean	SD		
NLR	3.82	1.09	1.95	0.86	-7.156	0.000
MLR	0.74	0.13	0.22	0.13	-8.046	0.000
PLR	144.46	71.64	126.13	62.74	-1.083	0.279

TABLE NO. 20 DISTRIBUTION OF INFLAMMATORY MARKERS AT WEEK 1.

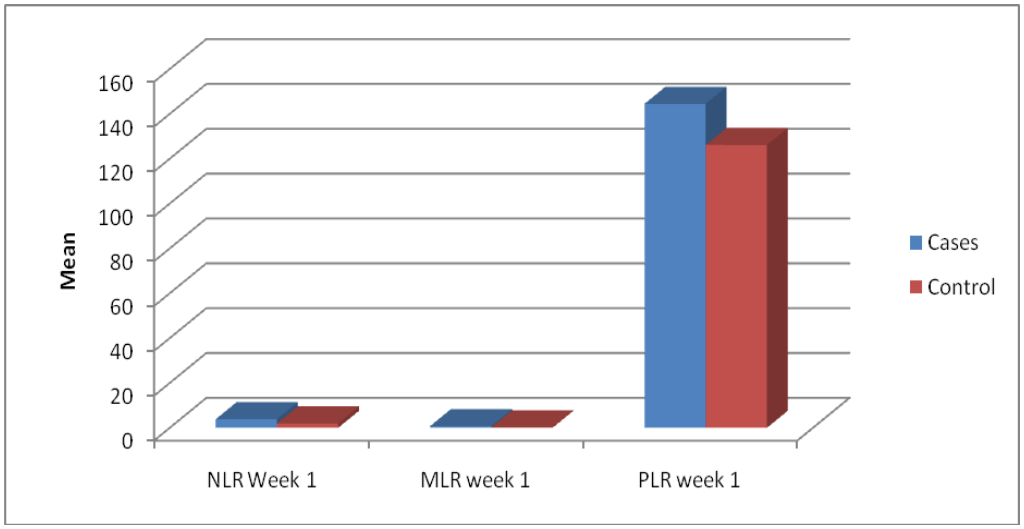

FIGURE NO. 20 DISTRIBUTION OF INFLAMMATORY MARKERS AT WEEK 1.

; Showsthat case had significantly higher NLR and MLR compared to controls, suggesting a higher inflammatory response in cases at week 1.

	CASES		CONTROL		Z	p-value
	Mean	SD	Mean	SD		
NLR	3.48	1.36	1.71	0.85	-6.559	0.000
MLR	0.79	0.27	0.19	0.10	-8.273	0.000
PLR	169.23	85.38	126.15	61.06	-2.813	0.005

TABLE NO. 21 DISTRIBUTION OF INFLAMMATORY MARKERS AT WEEK 3

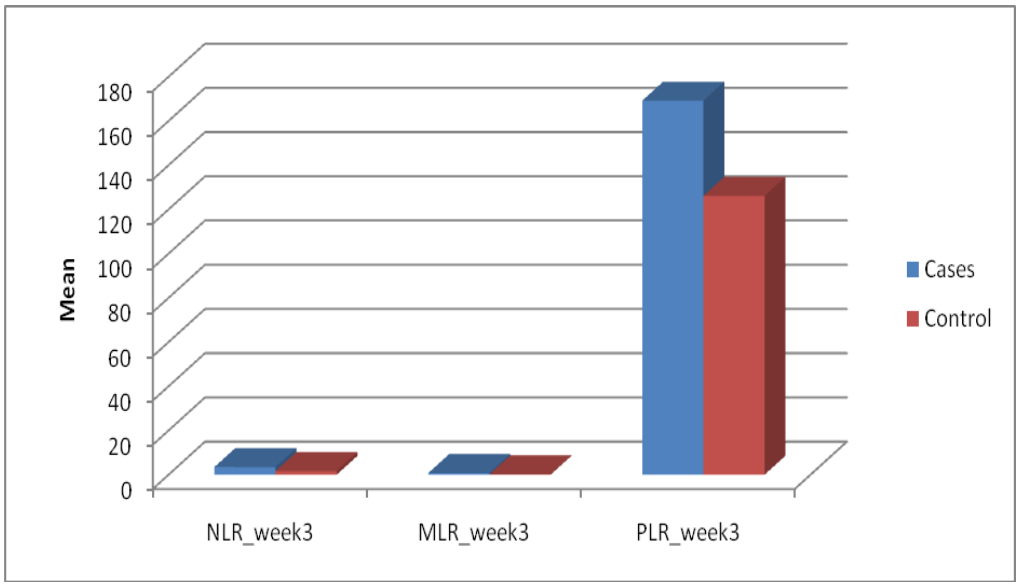

FIGURE NO. 21 DISTRIBUTION OF INFLAMMATORY MARKERS AT WEEK 3

; Shows that the cases had significantly higher NLR, MLR, and PLR compared to controls. This suggests a higher inflammatory response in cases at week 3

	CASES		CONTROL		Z	p-value
	Mean	SD	Mean	SD		
NLR	3.75	1.54	1.61	0.71	-7.504	0.000
MLR	0.73	0.12	0.18	0.11	-8.234	0.000
PLR	161.73	84.91	125.45	61.02	-2.404	0.016

TABLE NO. 22. DISTRIBUTION OF INFLAMMATORY MARKERS AT WEEK 16

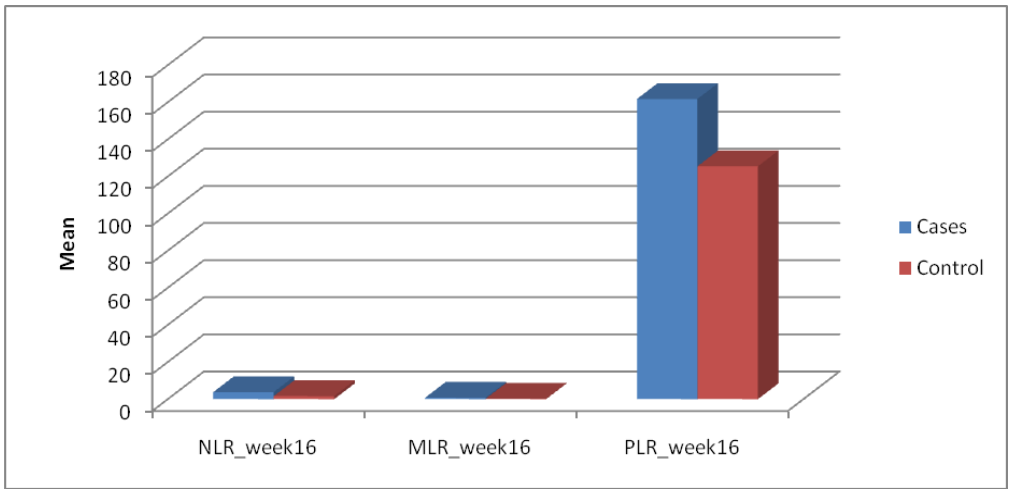

FIGURE NO. 22 DISTRIBUTION OF INFLAMMATORY MARKERS AT WEEK 16

; Shows that cases had significantly higher NLR, MLR,andPLR than controls at week 16. This suggests that cases exhibited higher levels of inflammation and immune system activation than controls.

	CASES		CONTROL		Z	p-value
	Mean	SD	Mean	SD		
Δ NLR	0.34	1.21	0.24	0.44	-0.393	0.694
Δ MLR	-0.05	0.28	0.02	0.06	-3.272	0.001
Δ PLR	-24.77	81.34	-0.02	4.63	-2.134	0.033

TABLE NO. 23 CHANGE IN INFLAMMATORY MARKERS FROM BASELINE TO 3 WEEKS

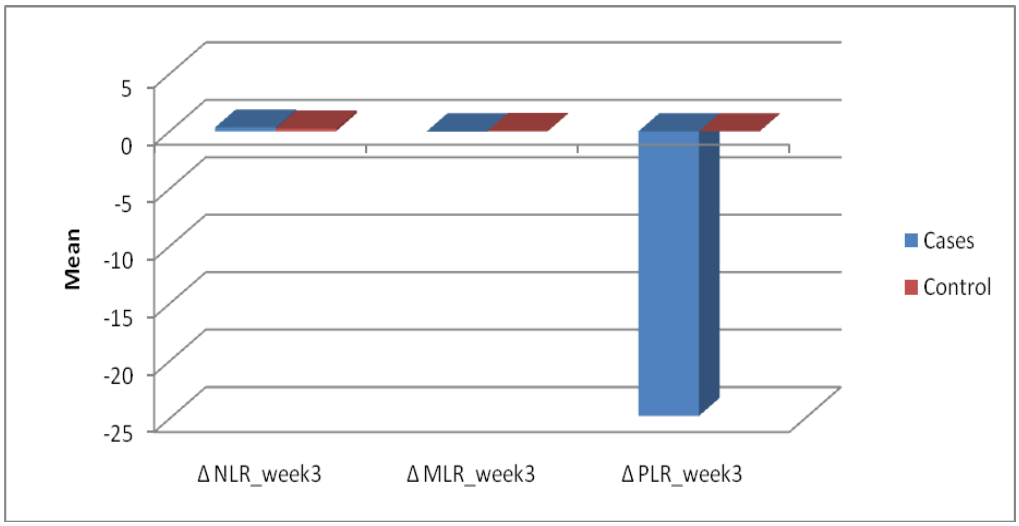

FIGURE NO. 23 CHANGE IN INFLAMMATORY MARKERS FROM BASELINE TO 3 WEEKS.

; Significant increase in MLR and PLR from baseline to 3 weeks shows that cases experienced increased inflammatory responses.

	CASES		CONTROL		Z	p-value
	Mean	SD	Mean	SD		
Δ NLR	0.08	1.19	0.35	0.56	-1.839	0.066
Δ MLR	0.01	0.14	0.03	0.06	-1.197	0.231
Δ PLR	-17.28	72.12	0.68	4.58	-1.542	0.123

TABLE NO. 24 CHANGE IN INFLAMMATORY MARKERS FROM BASELINE TO 16 WEEKS

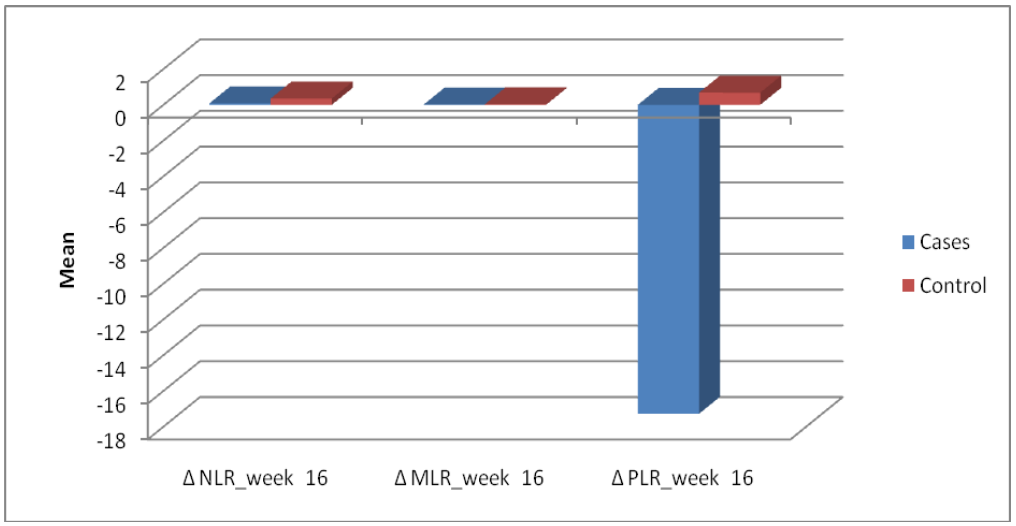

FIGURE NO. 24 CHANGE IN INFLAMMATORY MARKERS FROM BASELINE TO 16 WEEKS

; Shows that there were no significant differences in the change of neutrophil-to-lymphocyte ratio (Δ NLR), monocyte-to-lymphocyte ratio (Δ MLR), and platelet-to-lymphocyte ratio (Δ PLR) between cases and controls from baseline to 16 weeks

	SODIUM VALPROATE		LITHIUM		Z	p-value
	Mean	SD	Mean	SD		
NLR WEEK 1	3.72	0.97	3.91	1.18	-0.653	0.514
MLR WEEK 1	0.73	0.14	0.74	0.11	-0.875	0.382
PLR WEEK 1	135.37	68.12	151.60	74.10	-1.139	0.255
NLR WEEK 3	2.97	0.75	3.88	1.58	-2.673	0.008
MLR WEEK 3	0.77	0.39	0.80	0.11	-3.309	0.001
PLR WEEK 3	146.27	71.43	187.26	91.54	-2.465	0.014
NLRWEEK 16	3.00	0.66	4.33	1.76	-4.007	0.001
MLR WEEK 16	0.67	0.06	0.77	0.14	-2.896	0.004
PLR WEEK 16	125.80	29.33	189.96	102.27	-3.305	0.001
Δ NLR 3 WEEKS	0.75	1.21	0.02	1.12	-2.896	0.004
Δ MLR 3 WEEK	-0.04	0.41	-0.05	0.07	-1.819	0.069
Δ PLR 3 WEEK	-10.91	81.55	-35.66	80.23	-1.646	0.100
Δ NLR WEEK 16	0.72	0.97	-0.43	1.10	-4.458	0.000
Δ MLR WEEK 16	0.06	0.16	-0.02	0.11	-2.382	0.017
Δ PLRWEEK 16	9.56	72.83	-38.37	64.70	-2.715	0.007

TABLE NO. 25 COMPARISON OF INFLAMMATORY MARKERS AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

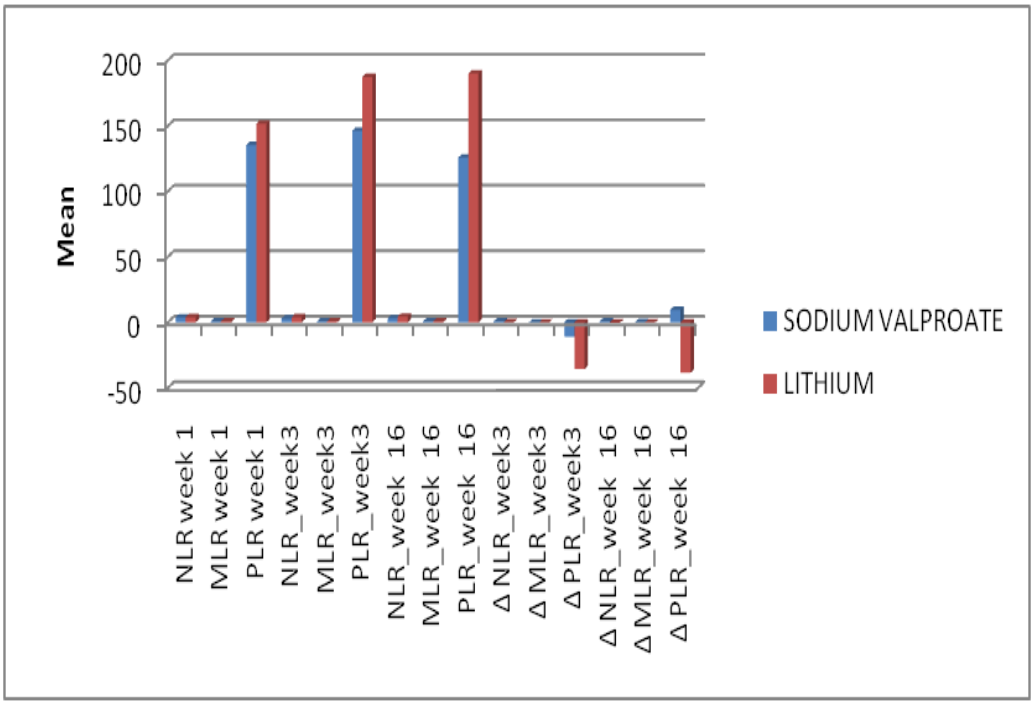

FIGURE NO. 25. COMPARISON OF INFLAMMATORY MARKERS AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

; Shows that patients in the lithium group had significantly higher baseline levels of inflammation and immune response markers (NLR, MLR, and PLR) at both week 3 and week 16 but patients treated with lithium showed a significantly larger decrease in NLR, MLR, and PLR by week 16

	SODIUM VALPROATE		LITHIUM		Z	p-value
	Mean	SD	Mean	SD		
TMT A WEEK 1	71.65	56.59	77.70	56.04	-0.534	0.595
TMT A WEEK 3	74.75	71.15	88.80	78.71	-0.924	0.358
TMT A WEEK 16	75.11	81.70	91.26	99.99	-0.867	0.388
ΔTMT A WEEK 3	-3.10	29.36	-11.10	35.53	1.205	0.231
Δ TMT A WEEK 16	-3.45	39.91	-13.55	56.50	1.005	0.318
TMT B WEEK 1	121.45	83.57	129.36	88.95	-0.453	0.652
TMT B WEEK 3	113.18	77.15	114.23	73.36	-0.069	0.945
TMT B WEEK 16	107.34	75.33	108.86	64.93	-0.108	0.914
Δ TMT B WEEK 3	8.27	16.68	15.13	34.32	-1.216	0.227
Δ TMT B WEEK 16	14.11	19.12	20.50	42.17	-0.931	0.354

TABLE NO. 26 COMPARISON OF TRAIL MAKING TESTS A AND B AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

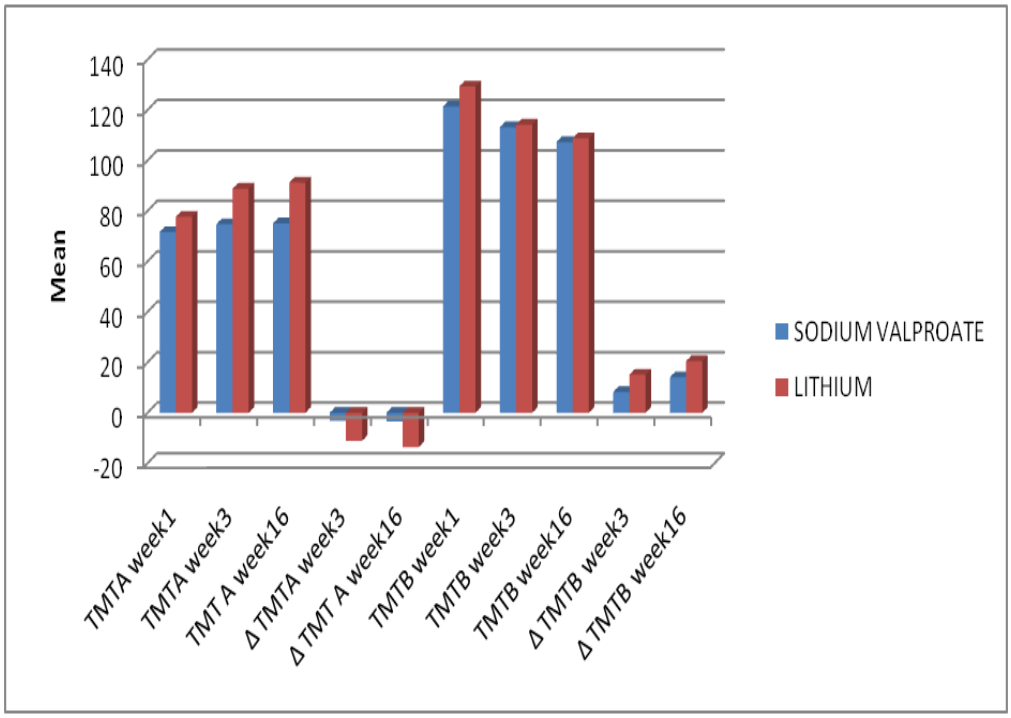

FIGURE NO. 26 COMPARISON OF TRAIL MAKING TEST A AND B AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

; Sodium valproate and lithium had similar effects on TMT A and TMT B duration over 16 weeks, with no significant differences in their duration or their changes over time.

	SODIUM VALPROATE		LITHIUM		Z	p-value
	Mean	SD	Mean	SD		
TOTAL SCORE OF MEMORY WEEK 1	82.16	12.48	87.96	11.06	-2.462	0.016
TOTAL SCORE OF MEMORY WEEK 3	81.68	13.54	87.55	11.29	-2.364	0.020
TOTAL SCORE OF MEMORY 16 WEEK	80.55	15.11	83.68	10.94	-1.202	0.232
Δ TOTAL SCORE OF MEMORY WEEK 3	0.48	2.65	0.41	2.81	0.121	0.904
Δ TOTAL SCORE OF MEMORY WEEK 16	1.61	5.31	4.29	4.96	-2.592	0.011

TABLE NO. 27 COMPARISON OF TOTAL SCORE OF MEMORY AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

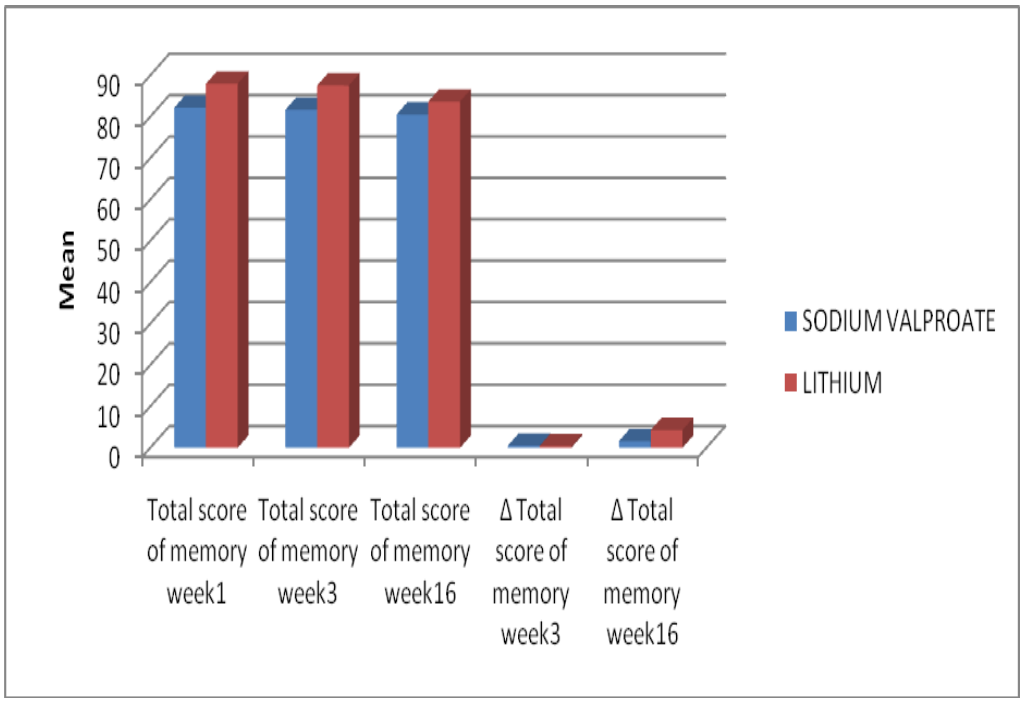

FIGURE NO. 27 COMPARISON OF TOTAL SCORE OF MEMORY AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

; Sodium valproate group had a total score of memory significantly lower than the lithium group at weeks 1, 3, and 16, with a significantly greater decline in total score of memory over 16 weeks observed in the lithium group than valproate.

	SODIUM VALPROATE		LITHIUM		Z	p-value
	Mean	SD	Mean	SD		
DSST WEEK 1	30.48	11.61	32.80	14.76	-0.857	0.393
DSST WEEK 3	29.93	12.23	31.64	14.16	-0.636	0.526
DSST WEEK 16	30.02	14.21	33.36	15.26	-1.118	0.266
Δ DSST WEEK 3	0.55	3.02	1.16	3.18	-0.982	0.329
Δ DSST WEEK 16	0.45	6.93	-0.55	7.25	0.703	0.483

TABLE NO. 28 COMPARISON OF DIGIT SYMBOL SUBSTITUTION TEST (DSST) AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

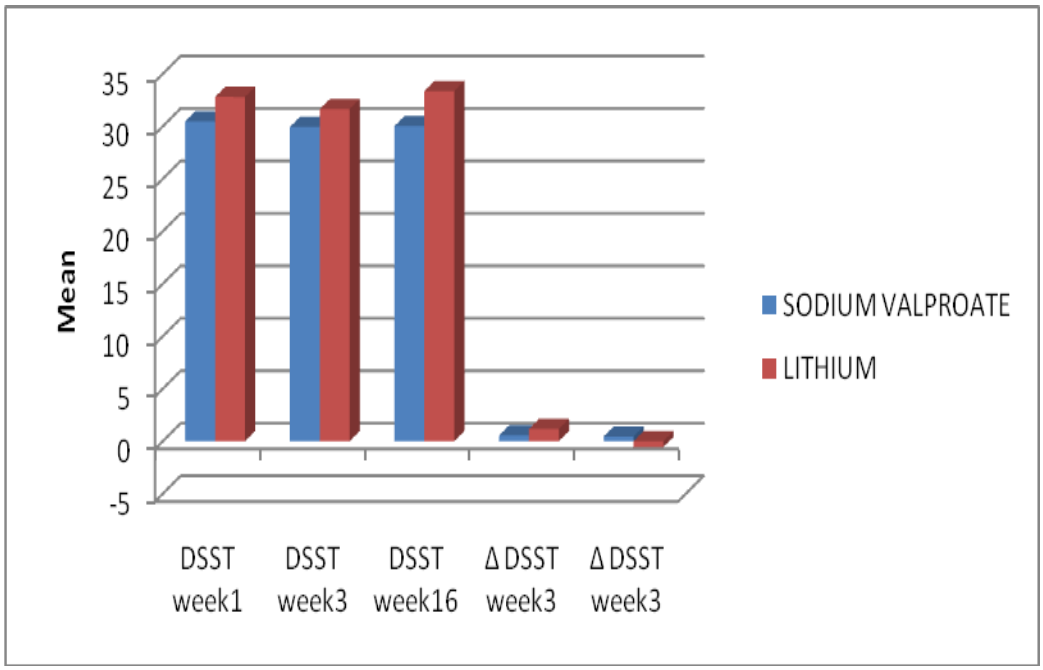

FIGURE NO. 28 COMPARISON OF DIGIT SYMBOL SUBSTITUTION TEST (DSST) AND MOOD STABILIZERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

; Sodiumvalproate and lithium had similar effects on DSST performance, with no significant differences over 16 weeks.

	FEMALE	MALE	Z	p-value
	Mean	Mean		
TMT A WEEK1	63.95	63.5	0.044	0.965
TMT A WEEK3	62.29	58.48	0.407	0.685
TMT AWEEK16	54.85	53.5	0.137	0.892
Δ TMT A WEEK3	1.66	5.02	-1.435	0.154
Δ TMT A WEEK16	9.1	10	-0.721	0.473
TMT B WEEK 1	135.77	121.43	0.767	0.445
TMT B WEEK 3	116.29	112.64	0.225	0.822
TMT B WEEK 16	113.03	106.01	0.466	0.642
Δ TMT B WEEK 3	19.48	8.8	1.781	0.078
Δ TMT B WEEK 16	22.74	15.42	0.995	0.322

TABLE NO 29. COMPARISON OF TMT A AND TMT B (TRAIL MAKING TEST) DURATION BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

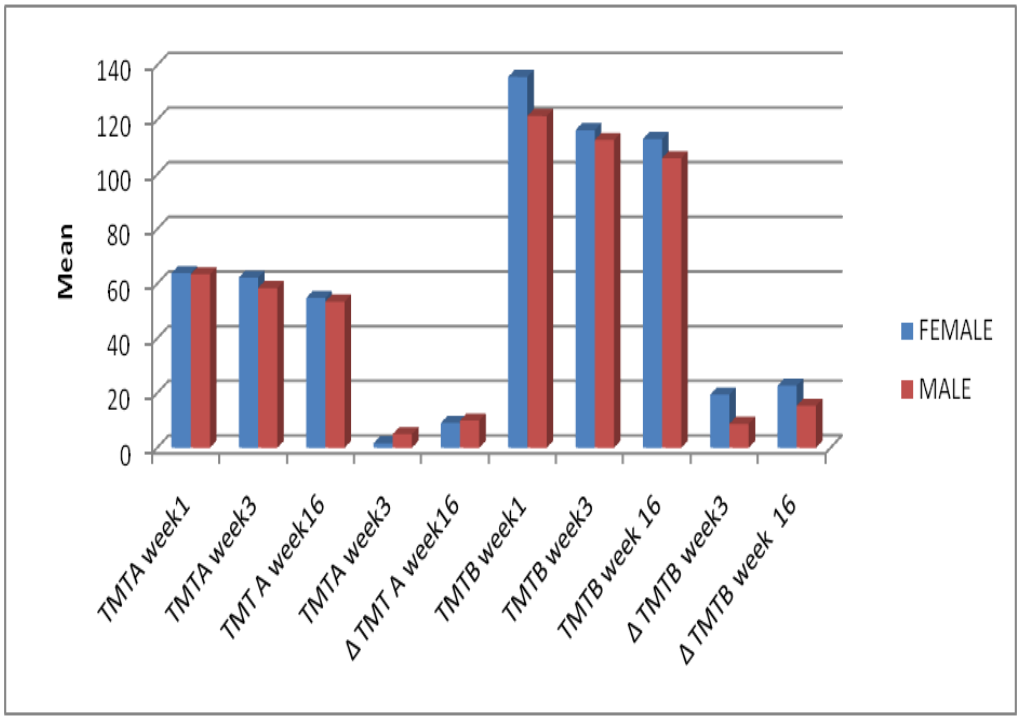

FIGURE NO 29. COMPARISON OF TMT A AND TMT B (TRAIL MAKING TEST) DURATION BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 AND 16 AND THE CHANGES FROM BASELINE TO WEEKS 3 AND 16.

;Nosignificant gender differences in TMT A and TMT B duration and change over time werefound.

	FEMALE		MALE		Z	p-value
	Mean	SD	Mean	SD		
TOTAL SCORE OF MEMORY WEEK1	88.68	11.39	83.94	12.06	1.847	0.068
TOTAL SCORE OF MEMORY WEEK 3	88.32	11.41	83.46	12.91	1.802	0.075
TOTAL SCORE OF MEMORY WEEK 16	84.65	10.82	81.25	13.76	1.216	0.227
Δ TOTAL SCORE OF MEMORY WEEK 3	0.35	2.78	0.48	2.72	-0.209	0.835
Δ TOTAL SCORE OF MEMORY WEEK 16	4.03	5.26	2.70	5.25	1.177	0.242

TABLE NO 30. COMPARISON OF TOTAL SCORE OF MEMORY BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

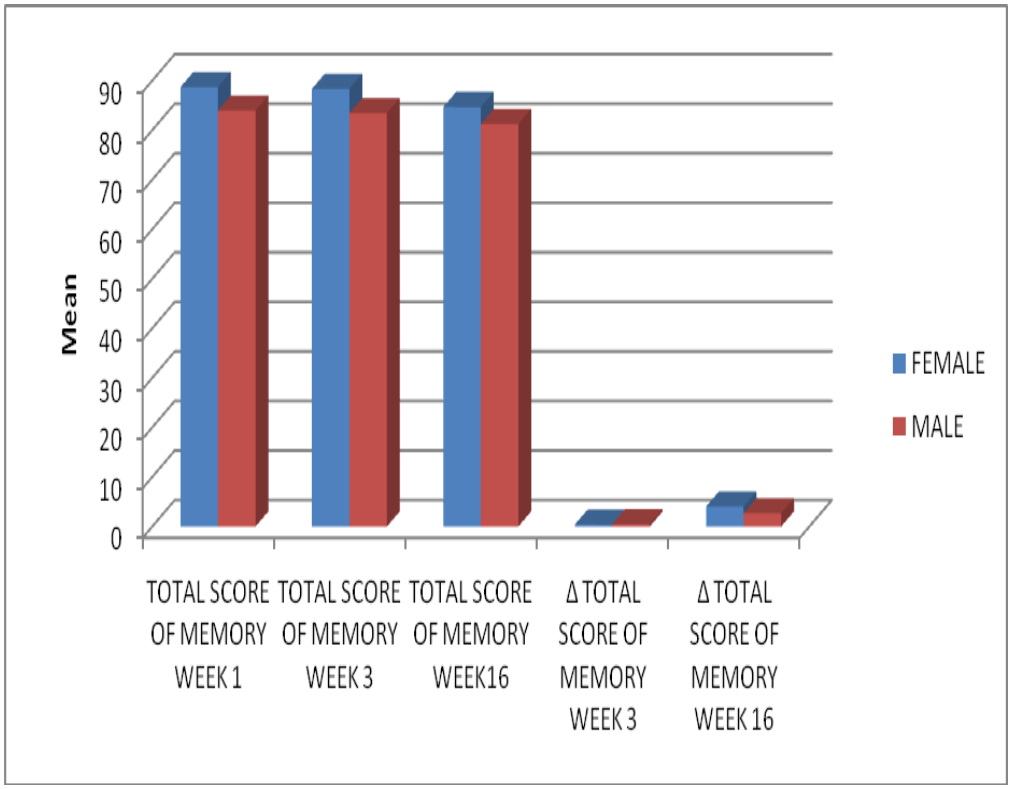

FIGURE NO. 30 COMPARISON OF TOTAL SCORE OF MEMORY BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

; Shows no significant gender differences between total score of memory at week 1, week 3, and week 16 or changes in memory scores over 16 weeks.

	FEMALE		MALE		Z	p-value
	Mean	SD	Mean	SD		
DSST WEEK 1	30.06	15.03	32.55	12.72	0.854	0.395
DSST WEEK 3	29.87	15.36	31.35	12.37	0.511	0.610
DSST WEEK 16	31.52	16.42	32.06	14.18	0.168	0.867
Δ DSST WEEK 3	0.19	1.96	1.20	3.48	1.511	0.134
Δ DSST WEEK 16	-1.45	6.09	0.49	7.47	1.271	0.207

TABLE NO 31. COMPARISON OF DIGIT SYMBOL SUBSTITUTION TEST (DSST) BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

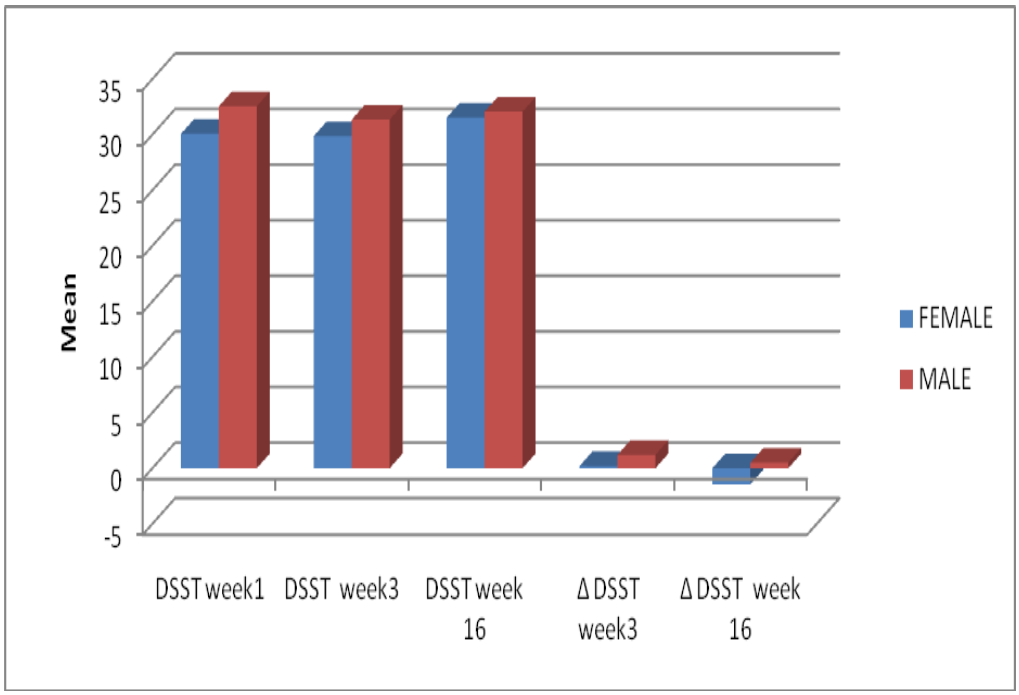

FIGURE NO 31. COMPARISON OF DIGIT SYMBOL SUBSTITUTION TEST (DSST) BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

; Indicates no significant gender differences between Digit Symbol Substitution Test (DSST) scores at week 1, week 3, and week 16 or changes in scores over 16 weeks.

	FEMALE		MALE		Z	p-value
	Mean	SD	Mean	SD		
NLR WEEK 1	4.05	1.23	3.72	1.02	1.394	0.167
MLR WEEK 1	0.73	0.10	0.74	0.14	-0.277	0.783
PLR WEEK 1	170.82	81.89	132.61	63.66	2.533	0.013
NLR WEEK 3	3.83	1.75	3.33	1.12	1.738	0.085
MLR WEEK 3	0.77	0.11	0.79	0.32	-0.339	0.735
PLR WEEK 16	202.38	83.01	154.33	82.74	2.683	0.009
NLR WEEK 16	4.33	1.77	3.48	1.35	2.645	0.010
MLR WEEK 16	0.78	0.13	0.70	0.11	2.914	0.004
PLR WEEK 16	211.29	112.84	139.47	57.07	4.233	0.000
Δ NLR WEEK 3	0.22	1.38	0.40	1.12	-0.677	0.500
Δ MLR WEEK 3	-0.04	0.08	-0.05	0.33	0.204	0.839
Δ PLR WEEK 3	-31.56	69.32	-21.72	86.50	-0.558	0.578
Δ NLR WEEK 16	-0.29	1.30	0.24	1.10	-2.082	0.040
Δ MLR WEEK 16	-0.04	0.11	0.04	0.14	-2.866	0.005
Δ PLR WEEK 16	-40.47	75.18	-6.86	68.73	-2.197	0.030

TABLE NO 32. COMPARISON OF MARKERS OF INFLAMMATION BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 ND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16

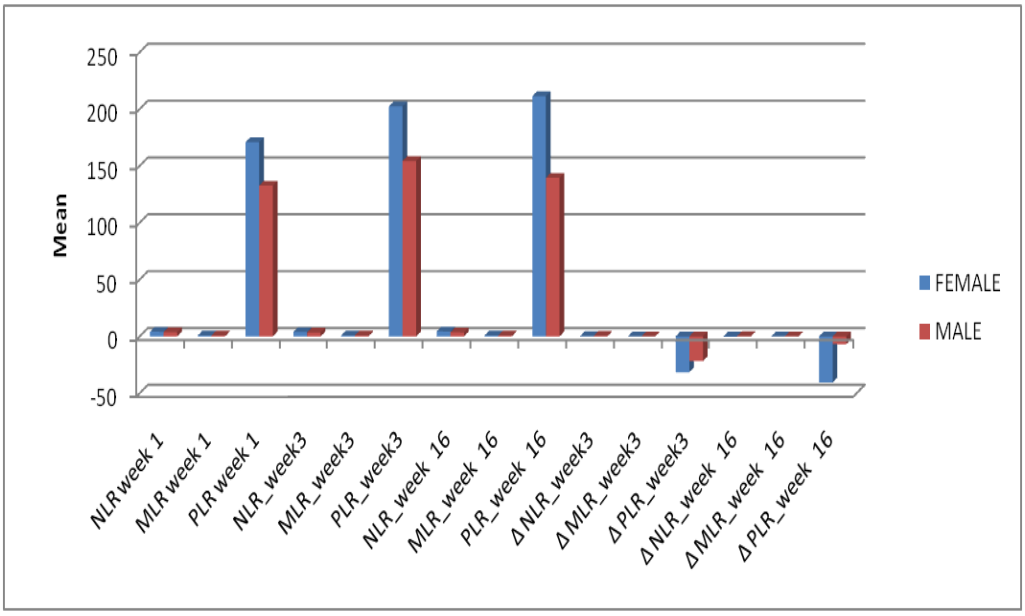

FIGURE NO 32. COMPARISON OF MARKERS OF INFLAMMATION BETWEEN FEMALE AND MALE PARTICIPANTS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16

; Shows that female initially exhibited significantly higher inflammatory markers (PLR, NLR, MLR) than males, but showed significant reductions in these markers over 16 weeks, indicating a more pronounced decrease in inflammation over time

Duration of illness	< 5		5-10.0		> 10		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
TMT A WEEK 1	52.61	23.93	81.15	83.98	93.70	54.10	6.01	0.003
TMT A WEEK 3	49.92	23.74	74.76	76.41	118.63	92.03	9.82	0.000
TMT A WEEK 16	44.61	23.64	71.67	82.56	129.25	117.70	10.12	0.000
Δ TMT A WEEK 3	2.69	11.84	6.39	11.24	-24.93	45.28	11.18	0.000
Δ TMT A WEEK 16	8.00	9.53	9.48	6.17	-35.55	70.84	11.31	0.000
TMT B WEEK 1	115.44	73.42	129.95	99.63	133.93	91.49	0.48	0.622
TMT B WEEK 3	105.97	66.54	116.33	82.99	120.03	78.75	0.36	0.698
TMT B WEEK 16	99.10	63.40	114.14	78.98	113.93	70.37	0.54	0.582
Δ TMT B WEEK 3	9.46	28.56	13.62	33.52	13.90	24.80	0.28	0.755
Δ TMT B WEEK 16	16.33	35.90	15.81	37.99	20.00	30.53	0.15	0.859

TABLE NO. 33 IMPACT OF DURATION OF ILLNESS ON TMT A AND TMT B DURATION (TRAIL MAKING TEST)AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16

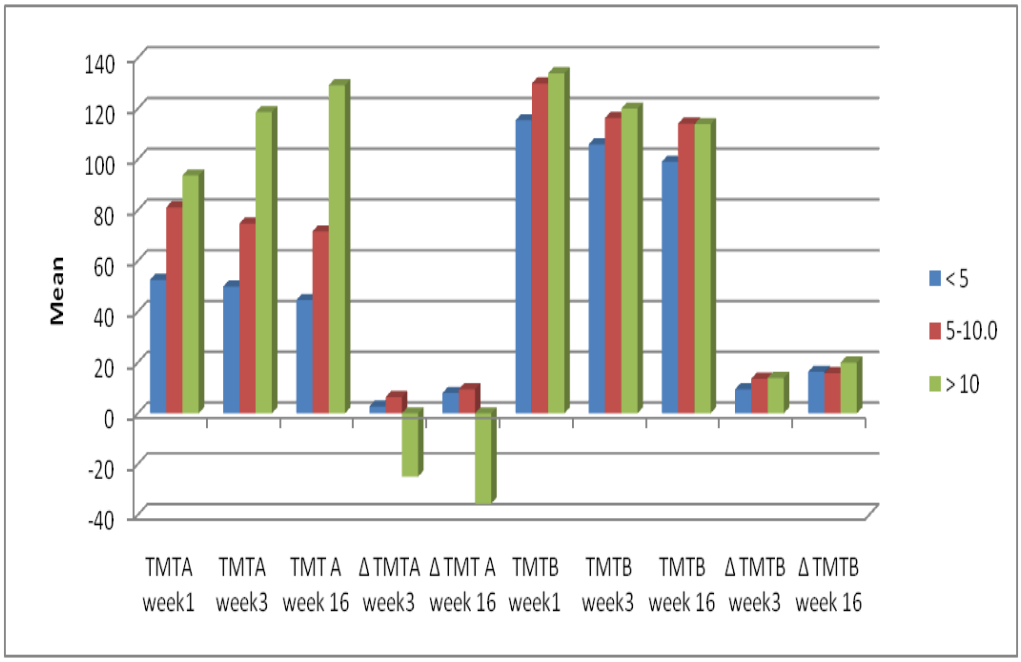

FIGURE NO. 33 IMPACT OF DURATION OF ILLNESS ON TMT A AND TMT B DURATION (TRAIL MAKING TEST) AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16

; Shows that the duration of illness significantly affected TMT A duration at weeks 1, 3, and 16 and its change (Δ TMTA) from baseline, with longer illness duration associated with a decline in cognitive processing speed and visual attention tasks (TMT A) over time.

DURATION OF ILLNESS	< 5		5-10.0		> 10		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
TOTAL SCORE OF MEMORY WEEK1	84.62	13.30	86.00	12.01	85.88	10.88	0.14	0.871
TOTAL SCORE OFMEMORY WEEK 3	83.92	14.22	85.33	12.87	85.80	10.94	0.23	0.798
TOTAL SCORE OF MEMORY 16 WEEK	81.18	14.86	82.10	12.26	83.50	11.47	0.32	0.730
Δ TOTAL SCORE OF MEMORY 3 WEEKS	0.69	2.13	0.67	2.67	0.08	3.25	0.59	0.554
Δ TOTAL SCORE OF MEMORY WEEK 16	3.44	4.51	3.90	4.12	2.38	6.39	0.70	0.499

TABLE NO. 34 IMPACT OF THE DURATION OF ILLNESS ON THE TOTAL SCORE OF MEMORY AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

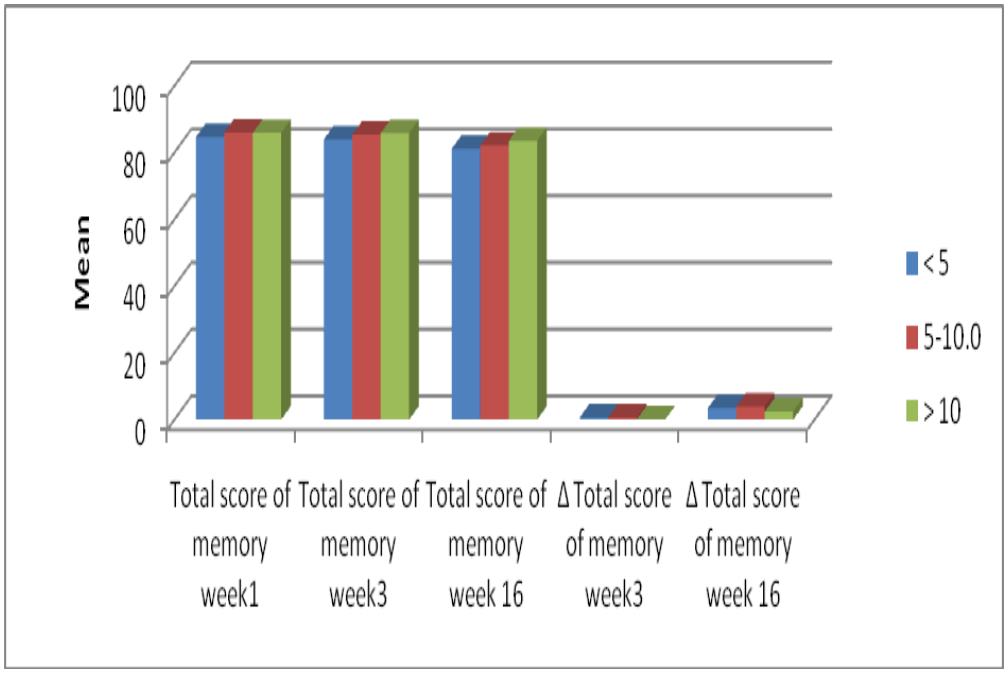

FIGURE NO. 34 IMPACT OF THE DURATION OF ILLNESS ON THE TOTAL SCORE OF MEMORY AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

; Shows that the duration of illness did not significantly affect the total score of memory at weeks 1, 3, and 16, nor did the changes in the total score of memory at 3 and 16 weeks.

DURATION OF ILLNESS	< 5		5-10.0		> 10		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
DSST WEEK 1	36.85	14.19	35.48	11.17	24.90	10.85	10.47	0.000
DSST WEEK 3	35.41	14.01	34.62	12.13	24.53	10.65	8.86	0.000
DSST WEEK 16	36.69	15.66	36.86	13.11	24.60	11.83	9.43	0.000
Δ DSST WEEK 3	1.44	3.99	0.86	3.29	0.38	1.72	1.15	0.320
Δ DSST WEEK 16	0.15	7.30	-1.38	8.82	0.30	5.90	0.43	0.655

TABLE NO. 35 THE IMPACT OF DURATION OF ILLNESS ON DIGIT SYMBOL SUBSTITUTION TEST (DSST) AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

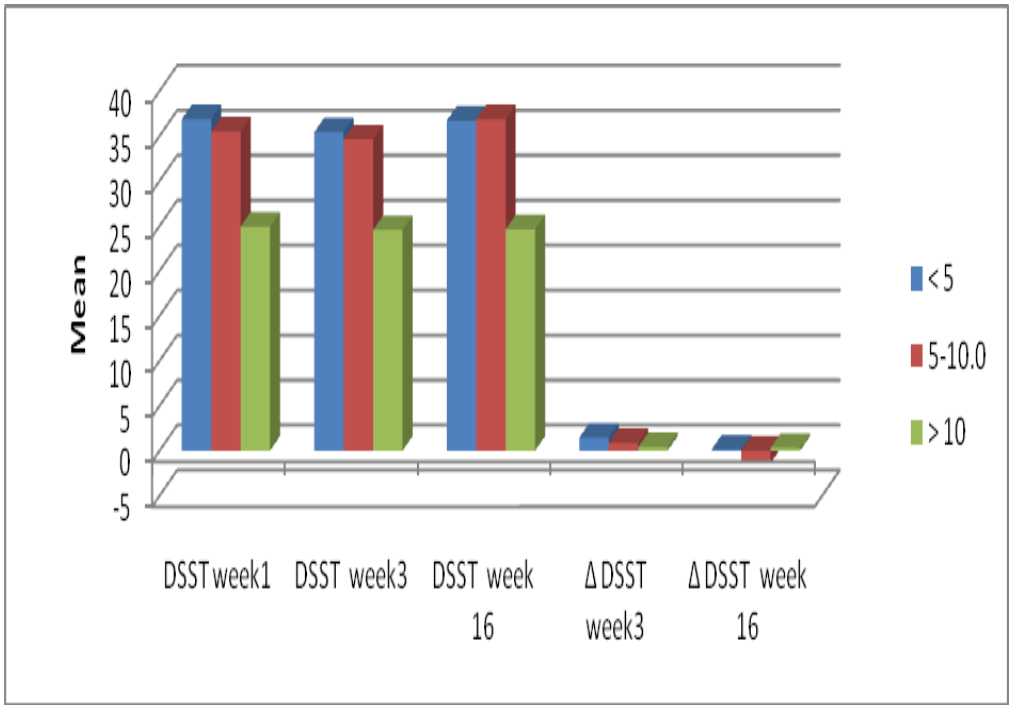

FIGURE NO. 35 THE IMPACT OF DURATION OF ILLNESS ON DIGIT SYMBOL SUBSTITUTION TEST (DSST) AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

; Indicates that the duration of illness significantly affected DSST scores at weeks 1, 3, and 16, with longer illness duration associated with lower DSST scores (all p=0.000), indicating a decline in processing speed and visual motor coordination.

DURATION OF ILLNESS	< 5		5-10.0		> 10		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
NLR WEEK 1	3.43	0.83	3.51	0.97	4.37	1.16	9.93	0.000
MLR WEEK 1	0.70	0.09	0.69	0.08	0.80	0.15	9.48	0.000
PLR WEEK 1	116.26	53.71	117.83	34.18	185.93	81.70	14.14	0.000
NLR WEEK 3	3.18	1.17	3.03	0.91	4.01	1.55	5.72	0.004
MLR WEEK 3	0.73	0.11	0.73	0.07	0.87	0.40	3.07	0.051
PLR WEEK 3	138.24	60.00	144.82	49.32	212.26	102.81	10.06	0.000
NLRWEEK 16	3.30	1.34	3.42	1.01	4.35	1.75	5.81	0.004
MLRWEEK 16	0.72	0.11	0.65	0.07	0.76	0.14	6.41	0.002
PLRWEEK 16	143.10	74.21	130.10	44.72	196.51	98.91	6.38	0.003
Δ NLR WEEK 3	0.25	1.06	0.47	1.48	0.36	1.20	0.23	0.795
Δ MLR WEEK 3	-0.03	0.11	-0.04	0.10	-0.06	0.42	0.13	0.874
Δ PLR WEEK 3	-21.98	77.08	-26.99	60.25	-26.33	95.57	0.04	0.963
Δ NLR WEEK 16	0.14	1.09	0.09	1.12	0.02	1.33	0.10	0.905
Δ MLR WEEK 16	-0.03	0.12	0.04	0.12	0.04	0.15	2.86	0.062
Δ PLR WEEK 16	-26.84	64.60	-12.27	58.65	-10.58	84.98	0.56	0.573

TABLE NO. 36 IMPACT OF DURATION OF ILLNESS ON INFLAMMATORY MARKERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16.

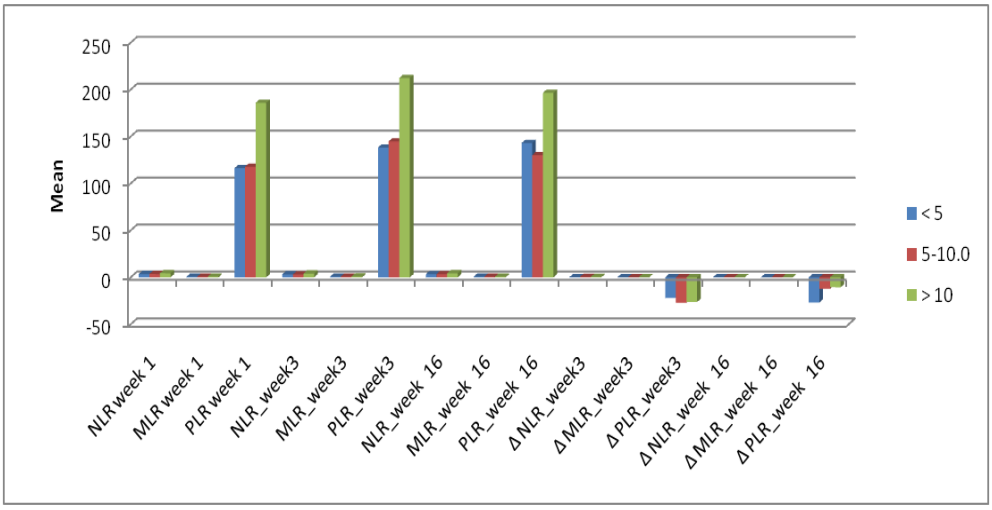

FIGURE NO. 36 IMPACT OF DURATION OF ILLNESS ON INFLAMMATORY MARKERS AT WEEKS 1,3 AND 16 AND THE CHANGE FROM BASELINE TO WEEKS 3 AND 16

; shows that the duration of illness significantly affected inflammatory markers (NLR, MLR, PLR) at weeks 1, 3, and 16, with longer illness duration associated with sustained inflammatory response.

Spearman's rho		DURATION OF ILLNESS (YEARS)	TMT A WEEK 1	TMT A WEEK 3	TMT A WEEK 16	ΔTMT A WEEK 3	ΔTMT A WEEK 16	TMT B WEEK 1	TMT B WEEK 3	TMT B WEEK 16	ΔTMT B WEEK 3	ΔTMT B WEEK 16
AGE	Correlation Coefficient	0.289	0.366	0.382	0.349	0.141	0.164	0.386	0.380	0.350	0.135	0.149
	p-value	0.003	0.000	0.000	0.000	0.162	0.102	0.000	0.000	0.000	0.180	0.138
DURATION OF ILLNESS (YEARS)	Correlation Coefficient		0.444	0.451	0.419	-0.183	-0.305	0.100	0.096	0.109	0.114	0.075
	p-value		0.000	0.000	0.000	0.068	0.002	0.323	0.344	0.281	0.257	0.459

TABLE NO. 37 (A) CORRELATION OF AGE, DURATION OF ILLNESS AND COGNITION

		TOTAL SCORE OF MEMORY WEEK 1	TOTAL SCORE OF MEMORY WEEK 3	TOTAL SCORE OF MEMORY WEEK 16	Δ TOTAL SCORE OF MEMORY WEEK 3	Δ TOTAL SCORE OF MEMORY WEEK 16	DSST WEEK 1	DSST WEEK 3	DSST WEEK 16	Δ DSST WEEK 3	Δ DSST WEEK 16
AGE	Correlation Coefficient	-0.316	-0.303	-0.245	0.035	-0.066	-0.021	-0.021	-0.054	0.034	0.025
	p-value	0.001	0.002	0.014	0.728	0.513	0.835	0.838	0.592	0.738	0.805
DURATION OF ILLNESS (YEARS)	Correlation Coefficient	0.038	0.042	0.040	-0.067	0.057	-0.426	-0.414	-0.382	-0.184	-0.086
	p-value	0.708	0.681	0.693	0.507	0.574	0.000	0.000	0.000	0.067	0.395

TABLE NO. 37 (B) CORRELATION OF AGE, DURATION OF ILLNESS AND COGNITION

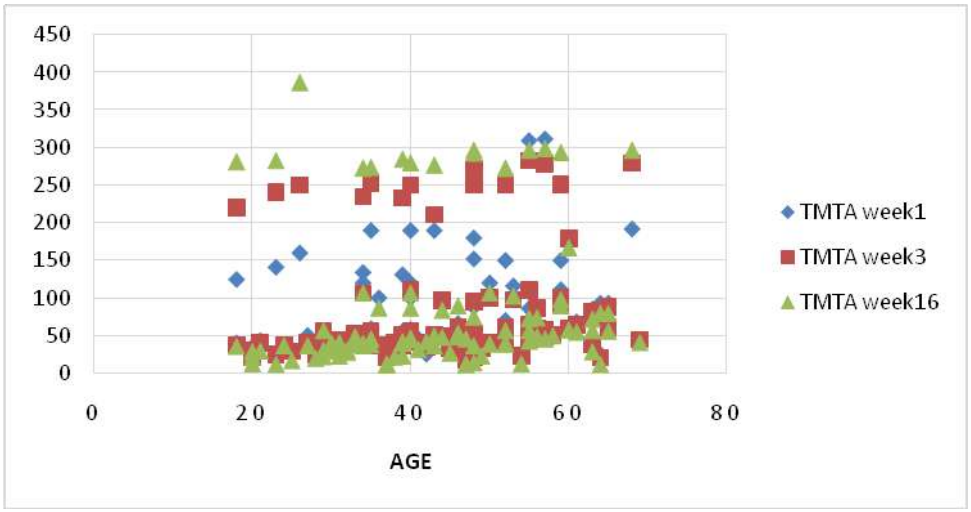

FIGURE NO. 37 (A) CORRELATION OF AGE AND TRAIL MAKING TEST A

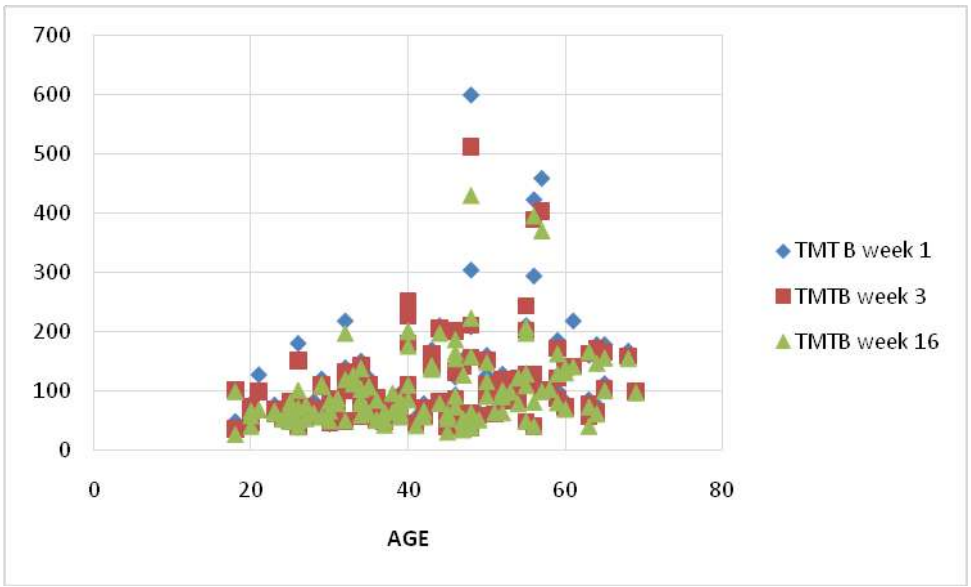

FIGURE NO. 37 (B) CORRELATION OF AGE AND TRAIL MAKING TEST B

; Shows significant positive correlations with TMTA and TMTB scores at different weeks, indicating that older age was associated with higher TMTA and TMTB scores.

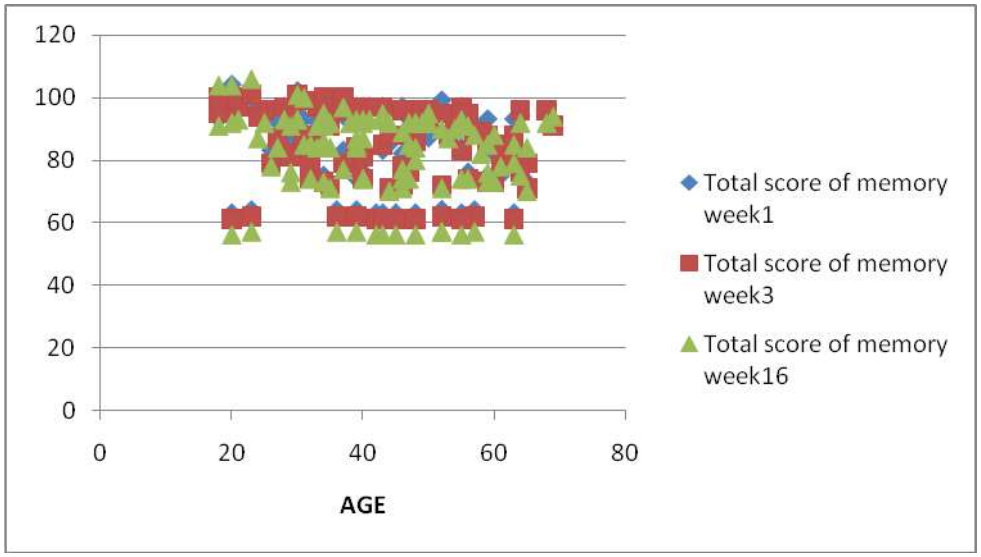

FIGURE NO. 37 (C) CORRELATION OF AGE AND TOTAL SCORE OF MEMORY

; age had significant negative correlations with the total score of memory at weeks 1, 3, and 16, indicating that memory performance declines with age

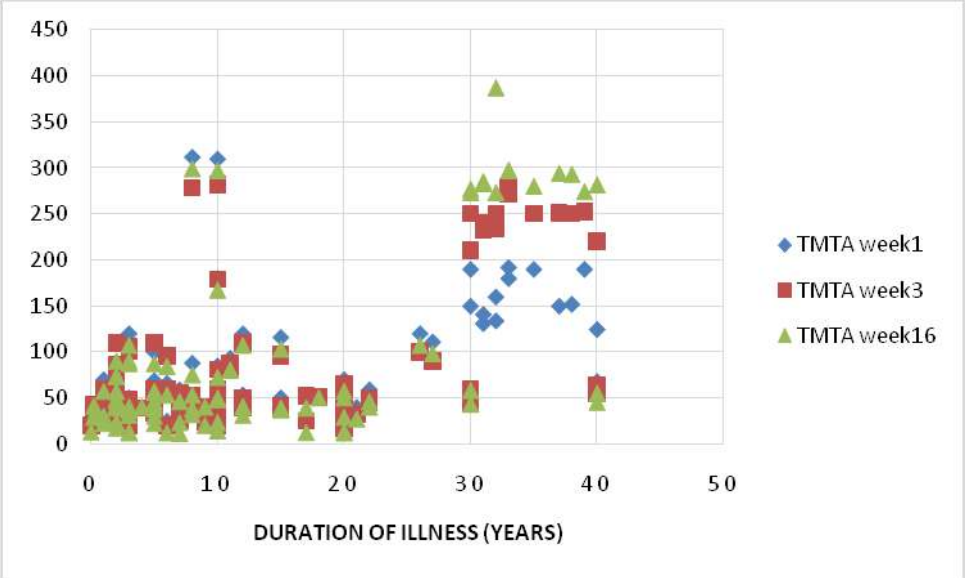

FIGURE NO. 37 (D) CORRELATION OF DURATION OF ILLNESS AND TMT A (TRAIL MAKING TEST A)

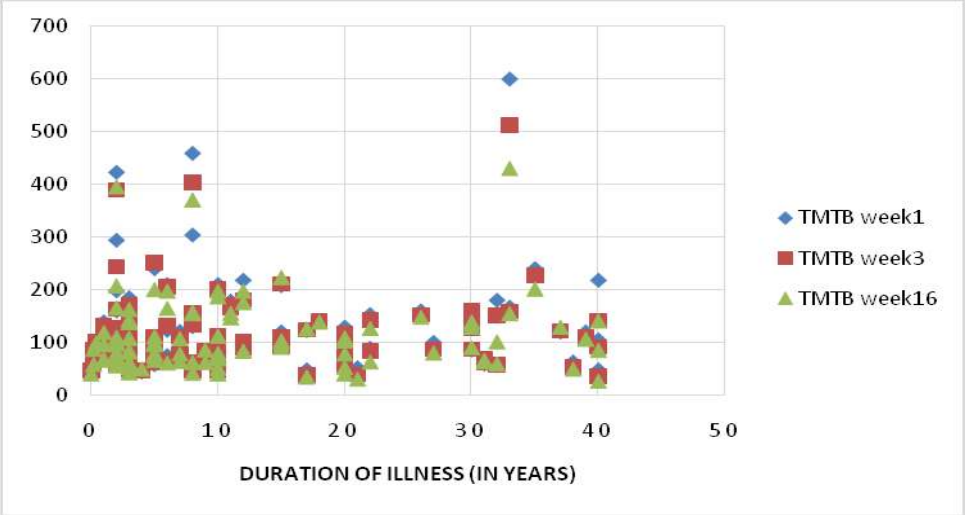

FIGURE NO. 37 (E) CORRELATION OF DURATION OF ILLNESS AND TMT B (TRAIL MAKING TEST B)

; Duration of illness (years) shows significant positive correlations with TMTA scores and a significant negative correlation with Δ TMTA WEEK 16, suggesting that longer illness duration was associated with higher initial TMT A scores but decreased over time.

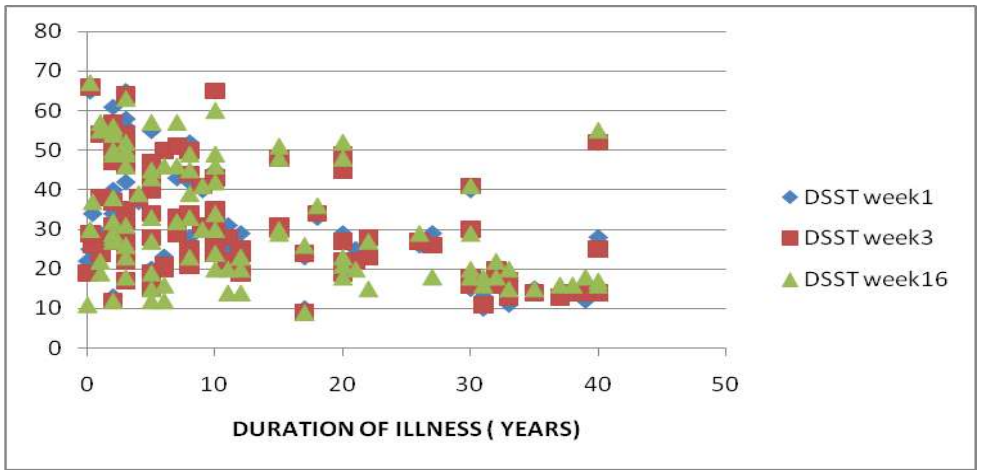

FIGURE NO. 37 (F) CORRELATION OF DURATION OF ILLNESS AND DIGIT SYMBOL SUBSTITUTION TEST SCORES (DSST)

; Duration of illness (years) shows significant negative correlations with DSST scores at weeks 1, 3, and 16, indicating that a longer duration of illness was associated with lower DSST scores, reflecting a decline in processing speed.

Spearman's rho	NLR WEEK 1	MLR WEEK 1	PLR WEEK 1	NLR WEEK 3	MLR WEEK 3	PLR WEEK 3	NLR WEEK 16	MLR WEEK 16	PLR WEEK 16
AGE	-0.014	0.115	0.041	0.096	0.113	0.079	0.006	-0.036	0.015
	0.891	0.255	0.683	0.342	0.265	0.434	0.951	0.719	0.885
DURATION OF ILLNESS(YEARS)	0.441	0.314	0.492	0.326	0.284	0.380	0.364	0.133	0.333
	0.000	0.001	0.000	0.001	0.004	0.000	0.000	0.187	0.001

TABLE NO. 38 (A) CORRELATION BETWEEN AGE, THE DURATION OF ILLNESS, AND INFLAMMATORY MARKERS

Spearman's rho		Δ NLR WEEK3	Δ MLR WEEK3	Δ PLR WEEK3	Δ NLR WEEK16	Δ MLR WEEK 16	Δ PLR WEEK 16
AGE	Correlation Coefficient	-0.063	0.053	-0.052	0.039	0.157	0.053
	p-value	0.534	0.600	0.609	0.697	0.119	0.602
DURATION OF ILLNESS (YEARS)	Correlation Coefficient	0.033	0.069	0.028	-0.035	0.172	0.056
	p-value	0.743	0.497	0.784	0.730	0.088	0.582

TABLE NO. 38 (B) CORRELATION BETWEEN AGE, THE DURATION OF ILLNESS,AND INFLAMMATORY MARKERS.

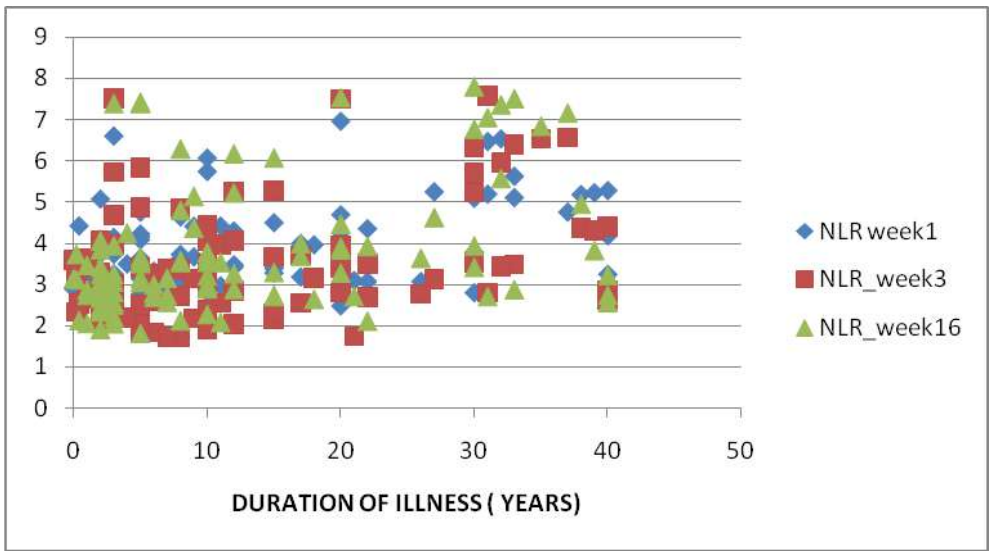

FIGURE NO. 38 (A) CORRELATION OF DURATION OF ILLNESS AND NLR.

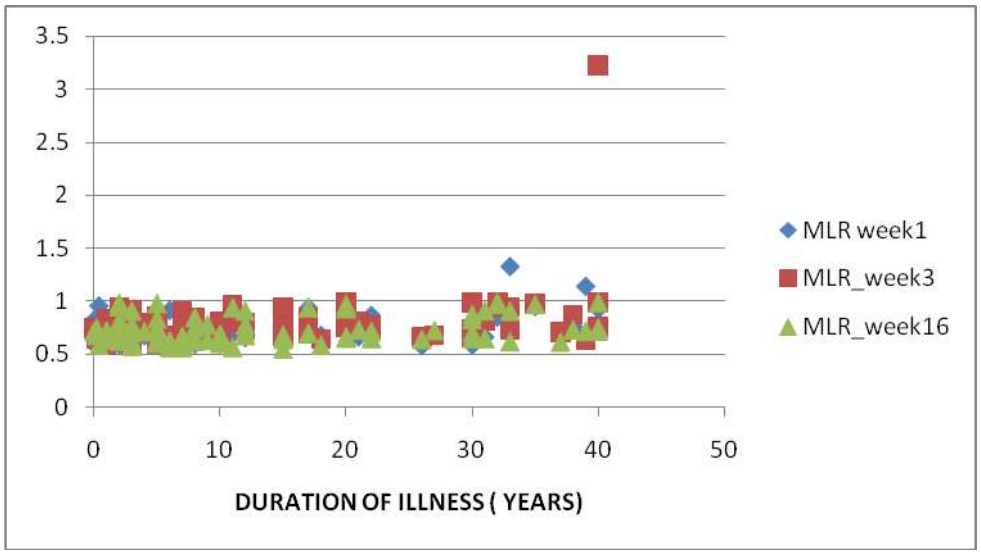

FIGURE NO. 38 (B) CORRELATION OF DURATION OF ILLNESS AND MLR

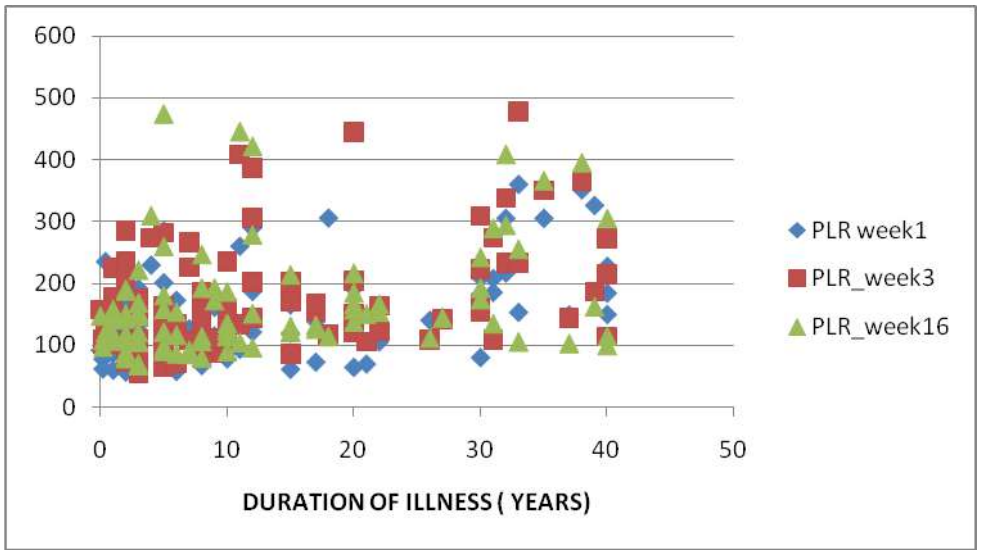

FIGURE NO. 38 (C) CORRELATION OF DURATION OF ILLNESS AND PLR

; Shows Duration of illness (years) had significant positive correlations with NLR, MLR, and PLR at weeks 1, 3, and 16, except for MLR at week 16, indicating that a longer duration of illness is associated with increased systemic inflammation

Spearman's rho		NLR WEEK 1	MLR WEEK 1	PLR WEEK 1	NLR WEEK 3	MLR WEEK 3	PLR WEEK 3	NLR WEEK 16	MLR WEEK 16	PLR WEEK 16
TMT A WEEK 1	Correlation Coefficient	0.211	0.185	0.245	0.177	-0.009	0.218	0.107	0.065	0.168
	p-value	0.035	0.066	0.014	0.079	0.930	0.029	0.288	0.521	0.095
TMT A WEEK 3	Correlation Coefficient	0.241	0.215	0.279	0.182	0.015	0.225	0.110	0.070	0.176
	p-value	0.016	0.032	0.005	0.071	0.884	0.024	0.277	0.487	0.079
TMT A WEEK 16	Correlation Coefficient	0.270	0.191	0.259	0.223	0.034	0.192	0.178	0.052	0.142
	p-value	0.007	0.057	0.009	0.026	0.737	0.056	0.076	0.604	0.158
Δ TMT A WEEK 3	Correlation Coefficient	-0.345	-0.238	-0.350	-0.230	-0.103	-0.141	-0.222	-0.119	-0.115
	p-value	0.000	0.017	0.000	0.022	0.306	0.162	0.026	0.240	0.255
Δ TMT A WEEK 16	Correlation Coefficient	-0.479	-0.193	-0.359	-0.305	-0.085	-0.173	-0.363	-0.068	-0.179
	p-value	0.000	0.055	0.000	0.002	0.398	0.086	0.000	0.504	0.075

TABLE NO. 39 (A) CORRELATION OF INFLAMMATORY MARKERS AND TMT A (TRAIL MAKING TEST)

Spearman's rho		Δ NLR WEEK 3	Δ MLR WEEK 3	Δ PLR WEEK 3	Δ NLR WEEK 16	Δ MLR WEEK 16	Δ PLR WEEK 16
TMT A WEEK 1	Correlation Coefficient	-0.013	0.182	-0.009	-0.013	0.067	-0.014
	p-value	0.895	0.070	0.925	0.896	0.506	0.890
TMT A WEEK 3	Correlation Coefficient	-0.012	0.185	0.002	-0.003	0.086	-0.002
	p-value	0.905	0.065	0.983	0.977	0.394	0.984
TMT A WEEK 16	Correlation Coefficient	-0.041	0.144	0.014	-0.058	0.072	0.015
	p-value	0.686	0.152	0.887	0.566	0.479	0.879
Δ TMT A WEEK 3	Correlation Coefficient	0.022	-0.076	-0.144	0.059	-0.007	-0.101
	p-value	0.828	0.454	0.152	0.560	0.943	0.317
Δ TMT A WEEK 16	Correlation Coefficient	0.028	-0.032	-0.130	0.132	-0.028	-0.051
	p-value	0.785	0.748	0.198	0.191	0.783	0.612

TABLE NO. 39 (B) CORRELATION OF INFLAMMATORY MARKERS AND TMT A (TRAIL MAKING TEST)

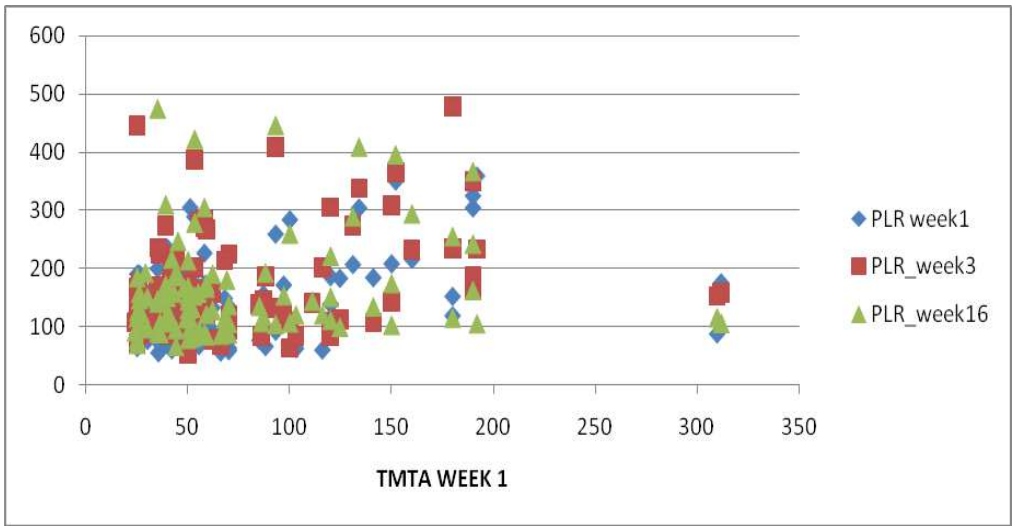

FIGURE NO. 39 (A) CORRELATION OF TMT A AT WEEK 1 AND PLR AT WEEKS 1,3 AND 16

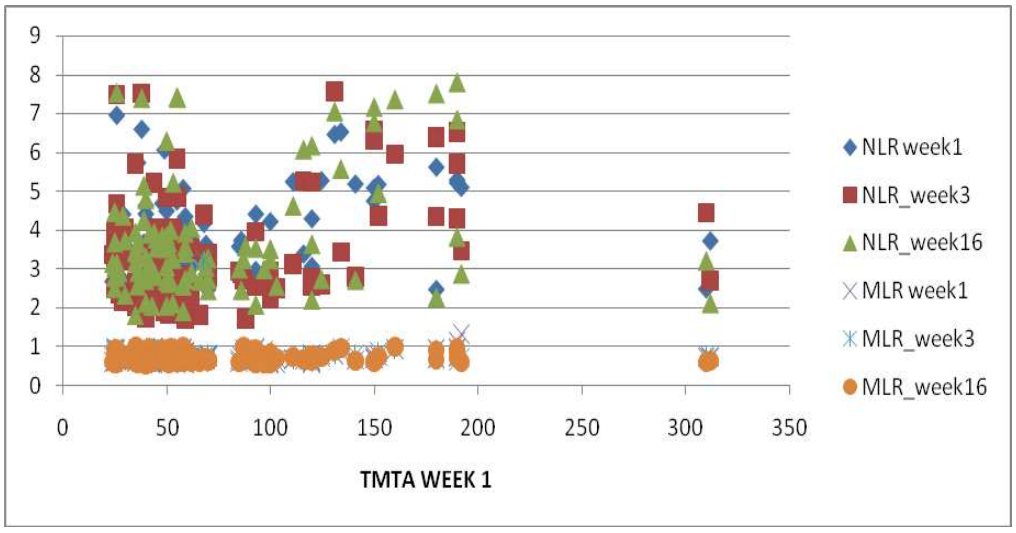

FIGURE NO.39 (B) CORRELATION OF TMT A AT WEEK 1 AND NLR AND MLR AT WEEKS 1,3 AND 16

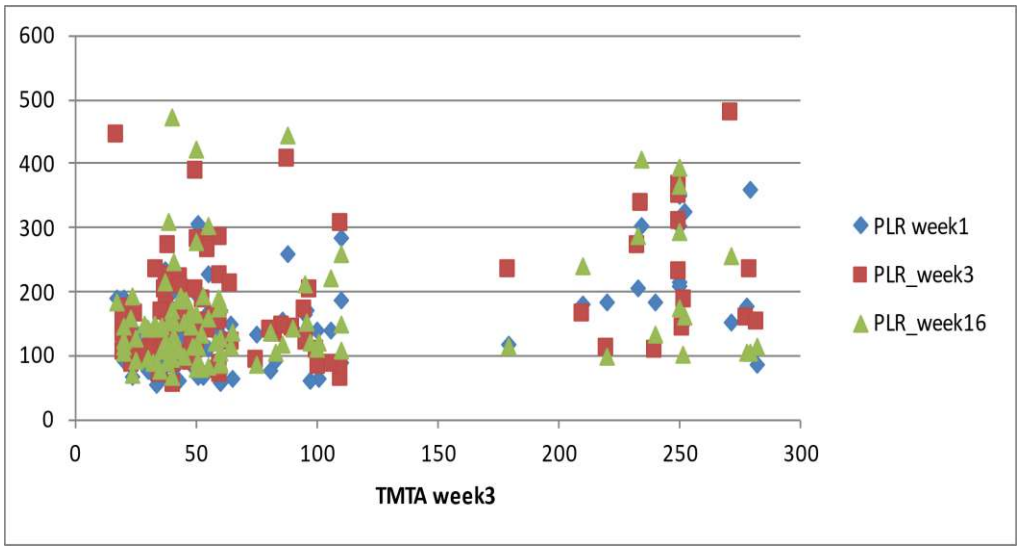

FIGURE NO.39 (C) CORRELATION OFTMT A AT WEEK 3 AND PLR AT WEEKS 1,3 AND 16

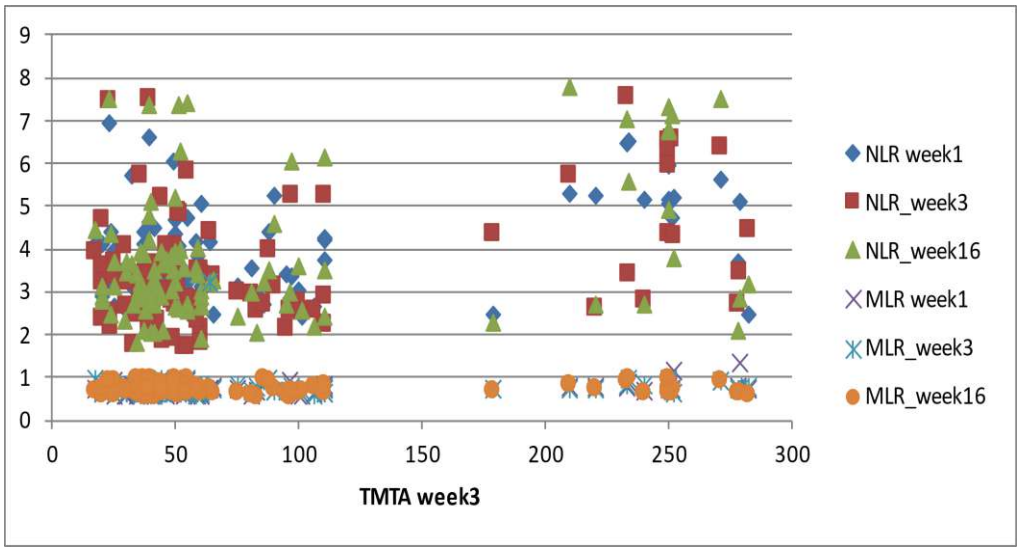

FIGURE NO. 39 (D) CORRELATION OF TMT A AT WEEK 3 AND NLR AND MLR AT WEEKS 1, 3 AND 16

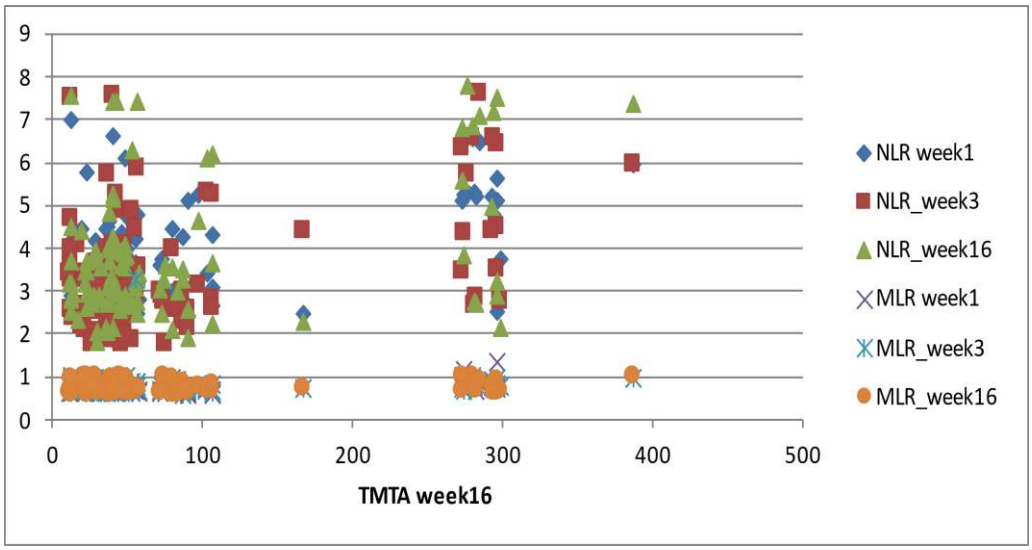

FIGURE NO. 39 (E) CORRELATION OF TMT A AT WEEK 16 AND NLR AND MLR AT WEEKS 1, 3 AND 16

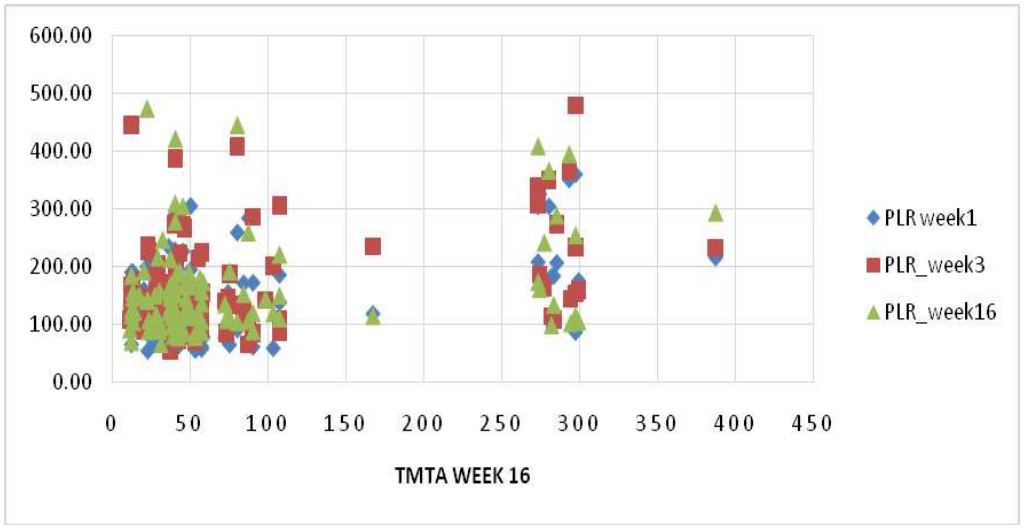

FIGURE NO. 39 (F) CORRELATION OF TMT A AT WEEK 16 AND PLR AT WEEKS 1, 3 AND 16

Higher levels of systemic inflammation were associated with worse cognitive processing speed and visual attention, as indicated by higher TMT A scores at weeks 1, 3, and 16.

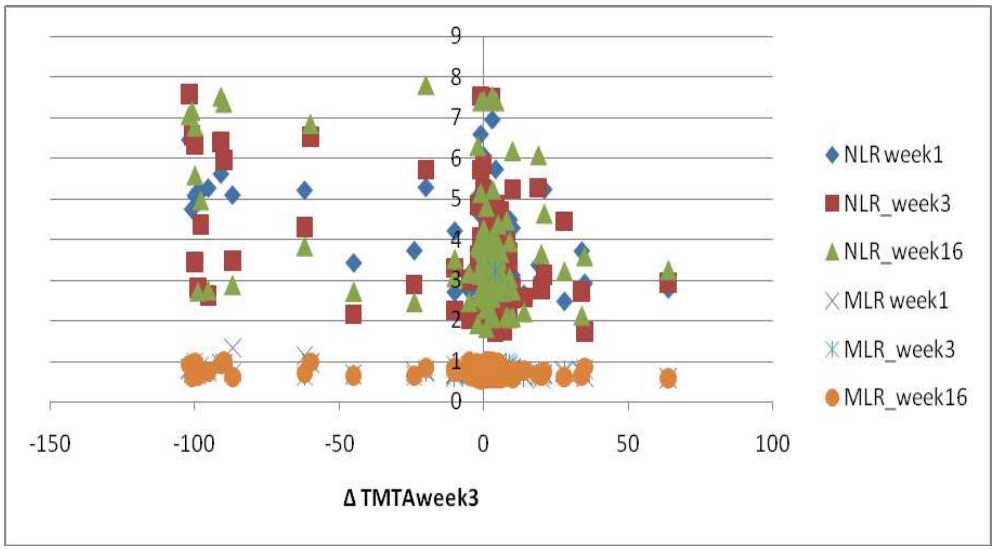

FIGURE NO.39 (G) CORRELATION OF CHANGE IN TMT A FROM BASELINE TO 3 WEEKS AND NLR AND MLR AT WEEK 1, WEEK 3, AND WEEK 16

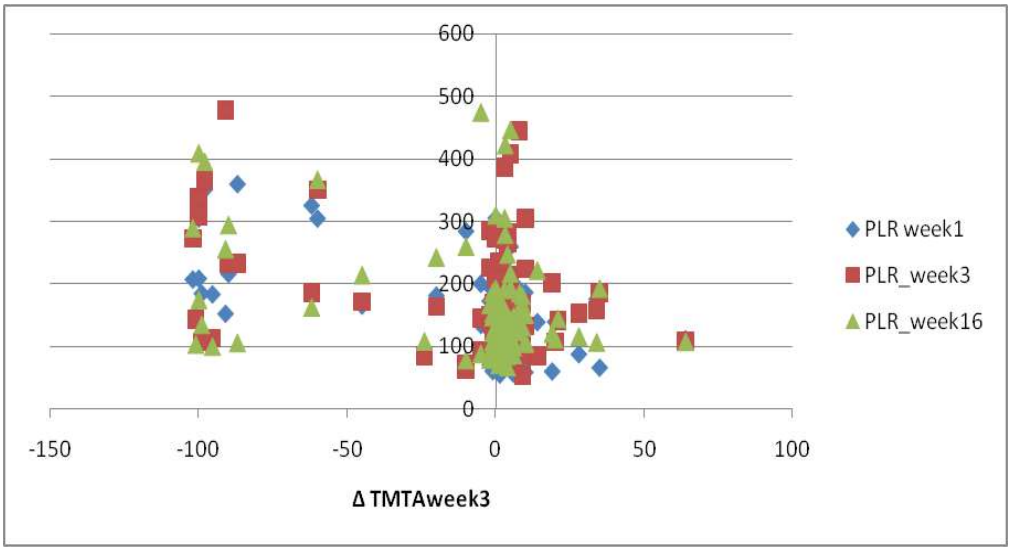

FIGURE NO. 39 (H) CORRELATION OF CHANGE IN TMT A FROM BASELINE TO 3 WEEKS AND PLR AT WEEK 1, WEEK 3, AND WEEK 16

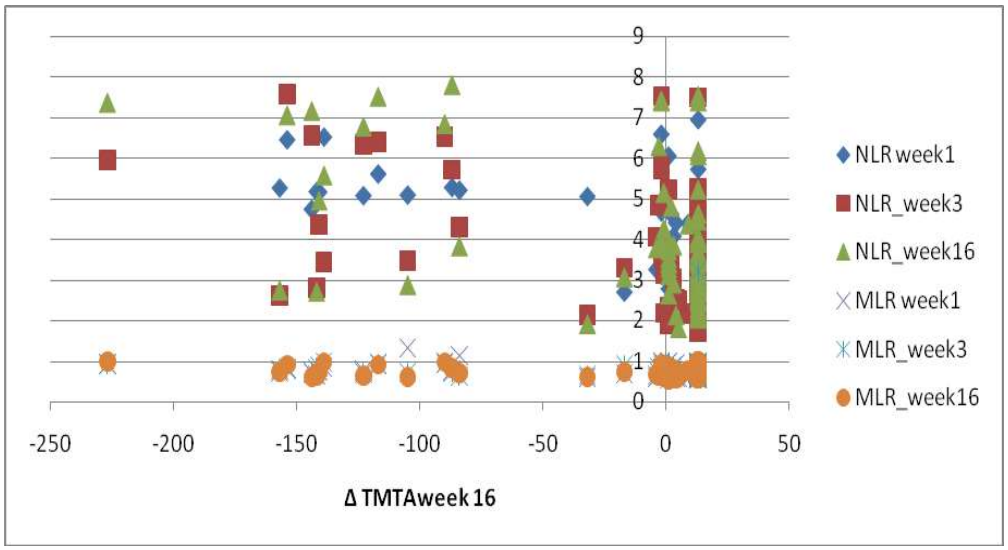

FIGURE NO. 39 (I) CORRELATION OF CHANGE IN TMT A FROM BASELINE TO 16 WEEKS AND NLR AND MLR AT WEEKS 1, 3 AND 16

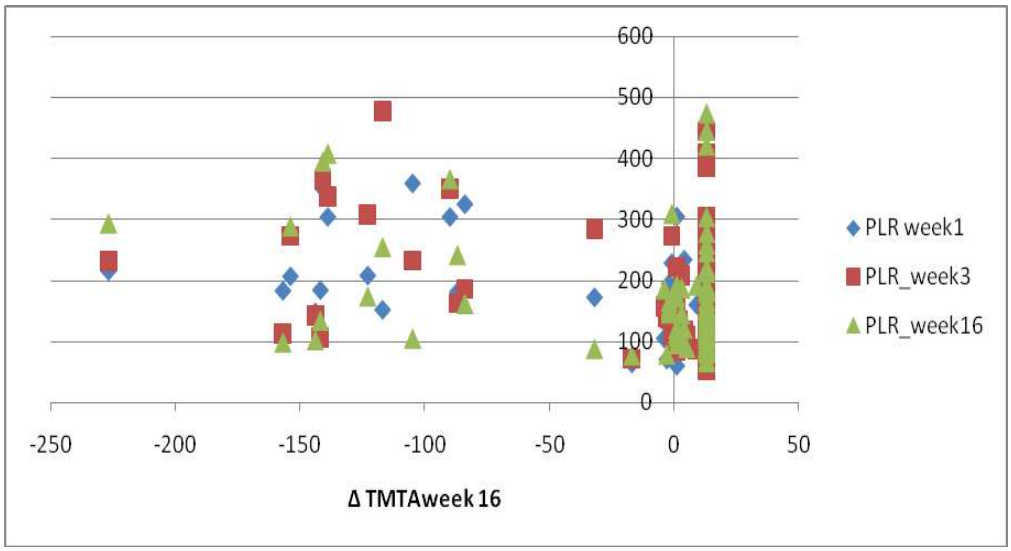

FIGURE NO.39 (J) CORRELATION OF CHANGE IN TMT A FROM BASELINE TO 16 WEEKS AND PLR AT WEEKS 1, 3 AND 16

; Changein TMT- A scores (Δ TMTA) at weeks 3 and 16 had significant negative correlations with these inflammation ratios.

Spearman's rho		NLR WEEK 1	MLR WEEK 1	PLR WEEK 1	NLR WEEK 3	MLR WEEK 3	PLR WEEK 3	NLR WEEK 16	MLR WEEK 16	PLR WEEK 16
TMT B WEEK 1	Correlation Coefficient	-0.040	0.073	0.017	0.032	-0.052	0.025	-0.046	-0.008	0.027
	p-value	0.692	0.471	0.866	0.751	0.610	0.804	0.652	0.940	0.788
TMT B WEEK 3	Correlation Coefficient	-0.010	0.090	0.037	0.071	-0.088	0.002	-0.014	-0.047	0.048
	p-value	0.922	0.371	0.715	0.481	0.385	0.986	0.888	0.640	0.635
TMT B WEEK 16	Correlation Coefficient	0.009	0.060	0.030	0.027	-0.114	-0.011	0.001	-0.082	0.027
	p-value	0.926	0.553	0.766	0.793	0.258	0.910	0.994	0.415	0.786
Δ TMT B WEEK 3	Correlation Coefficient	-0.093	0.070	-0.098	-0.073	0.194	0.147	-0.108	0.217	-0.017
	p-value	0.356	0.490	0.333	0.468	0.053	0.144	0.285	0.030	0.863
Δ TMT B WEEK16	Correlation Coefficient	-0.078	0.053	-0.043	-0.042	0.182	0.114	-0.138	0.266	0.072
	p-value	0.441	0.598	0.670	0.676	0.070	0.258	0.170	0.007	0.475

TABLE NO. 40 (A) CORRELATION OF INFLAMMATORY MARKERS AND TRAIL MAKING TEST B

Spearman's rho		Δ NLR WEEK 3	Δ MLR WEEK 3	Δ PLR WEEK 3	Δ NLR WEEK 16	Δ MLRWEEK 16	Δ PLRWEEK 16
TMTB WEEK 1	Correlation Coefficient	-0.092	0.137	-0.018	-0.031	0.068	0.011
	p-value	0.365	0.176	0.856	0.757	0.500	0.914
TMTB WEEK 3	Correlation Coefficient	-0.114	0.184	0.013	-0.058	0.114	-0.003
	p-value	0.259	0.068	0.898	0.567	0.259	0.978
TMTB WEEK 16	Correlation Coefficient	-0.072	0.180	0.015	-0.056	0.128	0.000
	p-value	0.475	0.073	0.879	0.582	0.203	0.997
ΔTMTB WEEK 3	Correlation Coefficient	0.051	-0.066	-0.206	0.085	-0.089	-0.080
	p-value	0.613	0.512	0.040	0.400	0.381	0.428
ΔTMTB WEEK 16	Correlation Coefficient	0.037	-0.067	-0.150	0.124	-0.153	-0.096
	p-value	0.715	0.508	0.136	0.220	0.128	0.342

TABLE NO. 40 (B) CORRELATION OF INFLAMMATORY MARKERS AND TRAIL MAKING TEST B

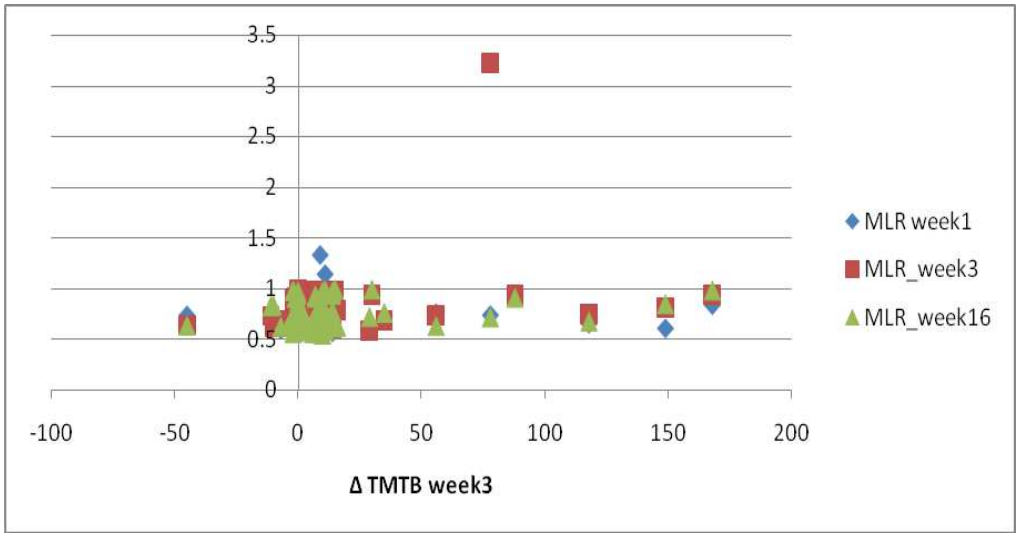

FIGURE NO. 40 (A) CORRELATION OF CHANGE IN TMT B FROM BASELINE TO 3 WEEKS AND MLR AT WEEKS 1, 3 AND 16

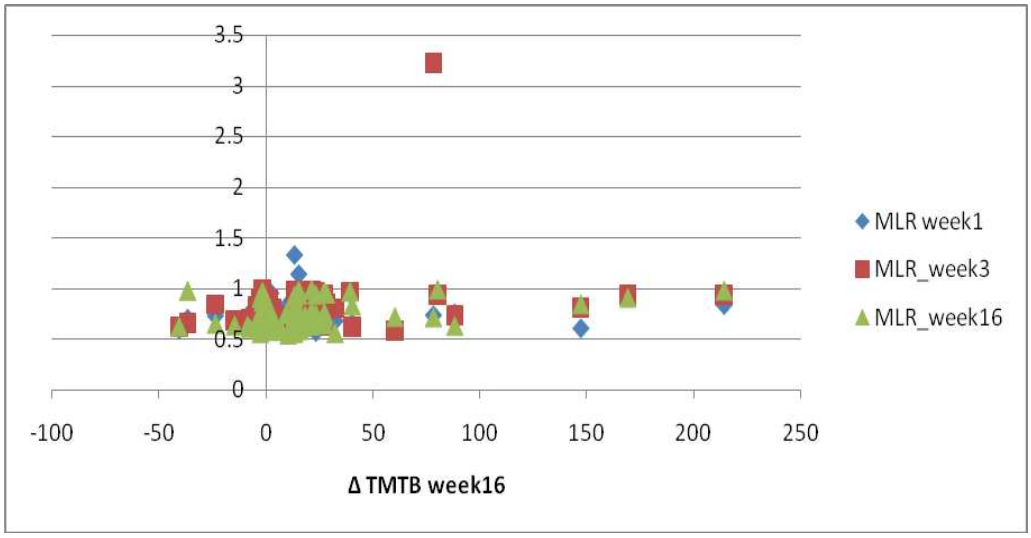

FIGURE NO. 40 (B) CORRELATION OF CHANGE IN TMT B FROM BASELINE TO 16 WEEKS AND MLR AT WEEKS 1, 3 AND 16

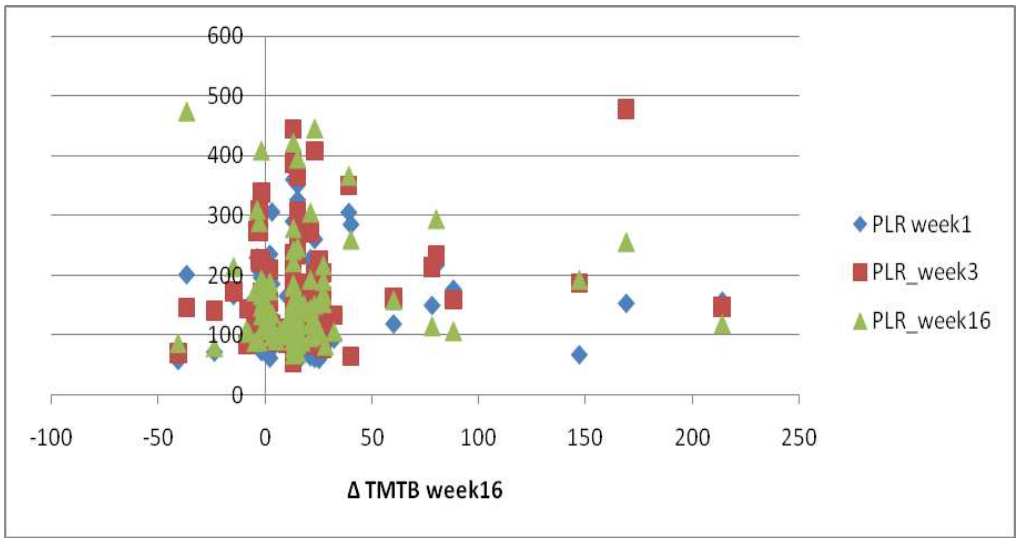

FIGURE NO. 40 (C) CORRELATION OF CHANGE IN TMT B FROM BASELINE TO 16 WEEKS AND PLR AT WEEKS 1, 3 AND 16

; Shows weak significant correlations of change in TMT B over 3 weeks with PLR at week 3 and change in TMTB at 16 weeks with MLR at week 16.

Spearman's rho		NLR WEEK 1	MLR WEEK 1	PLR WEEK 1	NLR WEEK 3	MLR WEEK 3	PLR WEEK 3	NLR WEEK 16	MLR WEEK 16	PLR WEEK 16
TOTAL SCORE OF MEMORY WEEK 1	Correlation Coefficient	0.064	0.077	0.097	0.116	-0.016	-0.014	0.219	0.118	0.154
	p-value	0.525	0.447	0.338	0.252	0.874	0.890	0.029	0.243	0.126
TOTAL SCORE OF MEMORY WEEK 3	Correlation Coefficient	0.036	0.051	0.110	0.049	-0.032	-0.054	0.172	0.110	0.134
	p-value	0.719	0.612	0.274	0.631	0.750	0.593	0.086	0.277	0.183
TOTAL SCORE OF MEMORY WEEK 16	Correlation Coefficient	0.024	-0.008	0.146	-0.025	-0.106	-0.101	0.097	0.051	0.114
	p-value	0.812	0.939	0.148	0.804	0.295	0.315	0.338	0.611	0.259
Δ TOTAL SCORE OF MEMORY WEEK 3	Correlation Coefficient	0.061	0.054	-0.096	0.194	0.095	0.107	0.089	-0.056	0.002
	p-value	0.546	0.591	0.341	0.053	0.347	0.288	0.376	0.581	0.988
Δ TOTAL SCORE OF MEMORY WEEK 16	Correlation Coefficient	0.085	0.160	-0.045	0.283	0.213	0.179	0.265	0.054	0.099
	p-value	0.400	0.113	0.659	0.004	0.034	0.075	0.008	0.595	0.325

TABLE NO. 41 (A) CORRELATION OF INFLAMMATORY MARKERS AND TOTAL SCORE OF MEMORY

Spearman's rho		Δ NLR WEEK 3	Δ MLR WEEK 3	Δ PLR WEEK 3	Δ NLR WEEK 16	Δ MLR WEEK 16	Δ PLR WEEK 16
TOTAL SCORE OF MEMORY WEEK 1	Correlation Coefficient	-0.061	0.067	0.050	-0.164	-0.043	-0.060
	p-value	0.550	0.510	0.618	0.102	0.672	0.552
TOTAL SCORE OF MEMORY WEEK 3	Correlation Coefficient	0.001	0.051	0.108	-0.105	-0.056	-0.044
	p-value	0.995	0.616	0.284	0.298	0.578	0.662
TOTAL SCORE OF MEMORY WEEK 16	Correlation Coefficient	0.069	0.077	0.168	-0.024	-0.040	0.004
	p-value	0.497	0.448	0.096	0.816	0.690	0.971
Δ TOTAL SCORE OF MEMORY WEEK 3	Correlation Coefficient	-0.190	0.022	-0.170	-0.170	0.104	-0.001
	p-value	0.058	0.826	0.090	0.090	0.302	0.995
Δ TOTAL SCORE OF MEMORY WEEK 16	Correlation Coefficient	-0.259	-0.020	-0.141	-0.297	0.063	-0.103
	p-value	0.009	0.845	0.162	0.003	0.534	0.307

TABLE NO. 41 (B) CORRELATION OF INFLAMMATORY MARKERS AND TOTAL SCORE OF MEMORY

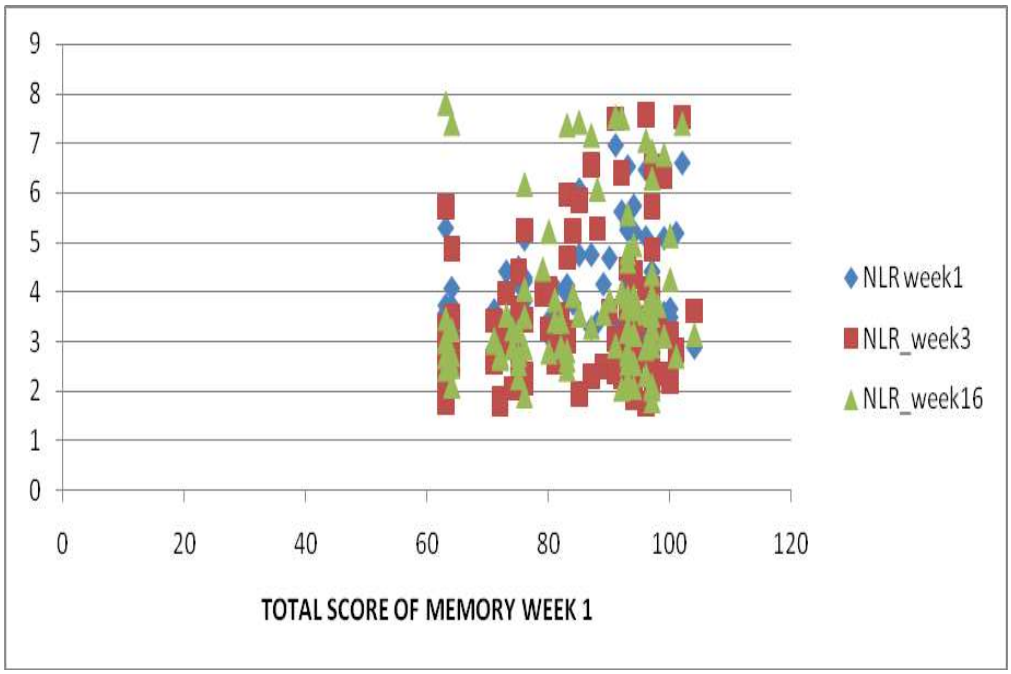

FIGURE NO. 41 (A) CORRELATION OF TOTAL SCORE OF MEMORY AT WEEK 1 AND NLR AT WEEKS 1, 3 AND 16

Higher inflammation markers (NLR, MLR, and PLR at week 3) were associated with lower memory scores at various points, indicating that elevated systemic inflammation negatively impacted memory performance over time.

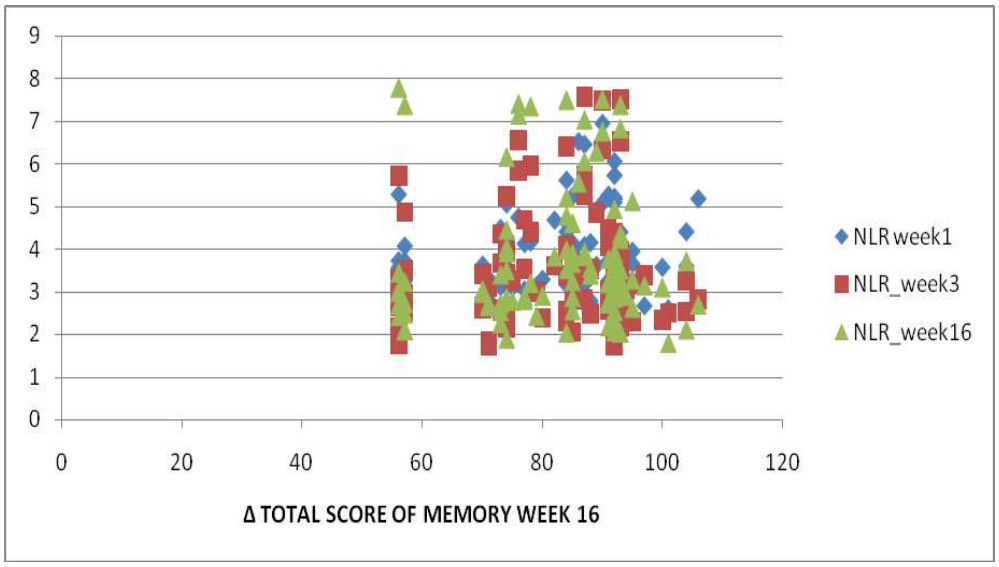

FIGURE NO. 41 (B) CORRELATION OF CHANGE IN TOTAL SCORE OF MEMORY FROM BASELINE TO WEEK 16 AND NLR AT WEEKS 1, 3 AND 16

FIGURE NO. 41 (C) CORRELATION OF CHANGE IN TOTAL SCORE OF MEMORY FROM BASELINE TO WEEK 16 AND MLR AT WEEKS 1, 3 AND 16

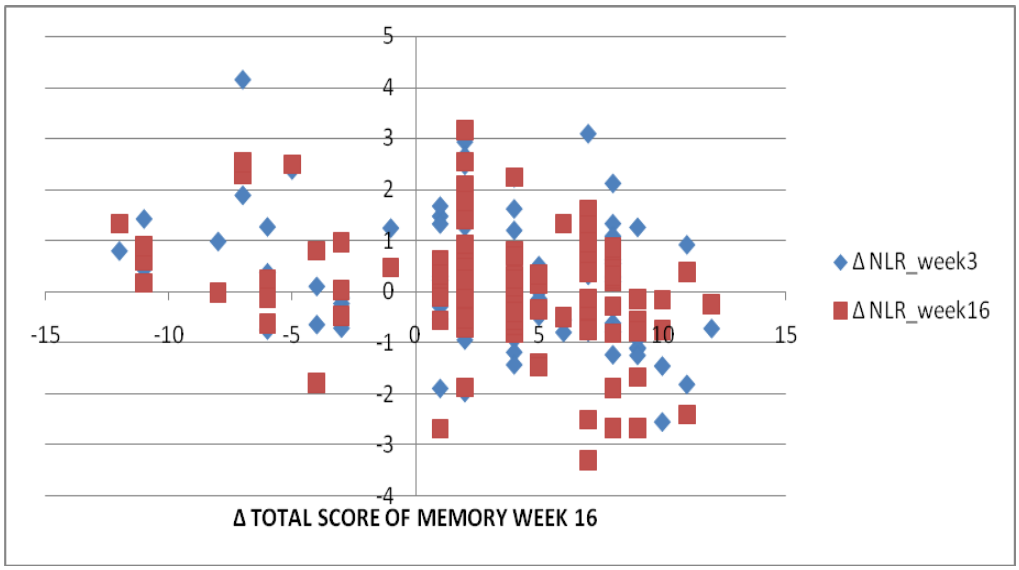

FIGURE NO. 41 (D) CORRELATION OF CHANGE IN TOTAL SCORE OF MEMORY FROM BASELINE TO WEEK 16 AND CHANGE IN NLR FROM BASELINE TO WEEK 3 AND WEEK 16

; Negative correlation between change in NLR at weeks 3 and 16 and changes in total memory scores, indicating that increases in NLR were associated with declines in memory performance over time.

TABLE NO 42 (A). CORRELATION OF INFLAMMATORY MARKERS AND DIGIT SYMBOL SUBSTITUTION TEST (DSST)

Spearman's rho		NLR WEEK1	MLR WEEK1	PLR WEEK1	NLR_WEEK3	MLR_WEEK3	PLR_WEEK3	NLR_WEEK 16	MLR_WEEK 16	PLR_WEEK 16
DSST WEEK 1	Correlation Coefficient	-0.223	-0.25	-0.41	-0.167	-0.09	-0.212	-0.268	-0.14	-0.294
	p-value	0.026	0.012	0	0.097	0.373	0.034	0.007	0.164	0.003
DSST WEEK 3	Correlation Coefficient	-0.209	-0.263	-0.394	-0.161	-0.08	-0.17	-0.252	-0.132	-0.288
	p-value	0.037	0.008	0	0.11	0.427	0.092	0.011	0.19	0.004
DSST WEEK 16	Correlation Coefficient	-0.217	-0.272	-0.342	-0.12	-0.096	-0.17	-0.225	-0.107	-0.225
	p-value	0.03	0.006	0	0.232	0.344	0.09	0.025	0.289	0.024
Δ DSST WEEK 3	Correlation Coefficient	-0.22	0	-0.21	-0.049	0.02	-0.188	-0.09	0.02	-0.031
	p-value	0.028	0.996	0.036	0.627	0.846	0.062	0.373	0.844	0.761
Δ DSST WEEK 3	Correlation Coefficient	-0.084	0.012	-0.161	-0.032	0.069	-0.034	-0.001	0.023	-0.035
	p-value	0.404	0.903	0.109	0.753	0.492	0.737	0.989	0.824	0.732

TABLE NO 42(B). CORRELATION OF INFLAMMATORY MARKERS AND DIGIT SYMBOL SUBSTITUTION TEST (DSST)

Spearman's rho		Δ NLR WEEK 3	Δ MLR_ WEEK 3	Δ PLR_ WEEK 3	Δ NLR_ WEEK 16	Δ MLR_ WEEK 16	Δ PLR_ WEEK16
DSST WEEK 1	Correlation Coefficient	0	-0.138	-0.137	0.109	-0.088	-0.086
	p-value	0.997	0.169	0.174	0.282	0.385	0.393
DSST WEEK 3	Correlation Coefficient	-0.005	-0.155	-0.155	0.098	-0.106	-0.083
	p-value	0.963	0.124	0.123	0.331	0.295	0.411
DSST WEEK 16	Correlation Coefficient	-0.047	-0.16	-0.096	0.03	-0.159	-0.097
	p-value	0.641	0.111	0.342	0.765	0.114	0.339
Δ DSST WEEK 3	Correlation Coefficient	-0.077	-0.019	-0.044	-0.026	0.014	-0.097
	p-value	0.446	0.854	0.667	0.796	0.888	0.339
Δ DSST WEEKS 16	Correlation Coefficient	-0.015	-0.045	-0.139	0.008	0.042	-0.066
	p-value	0.88	0.656	0.169	0.937	0.68	0.512

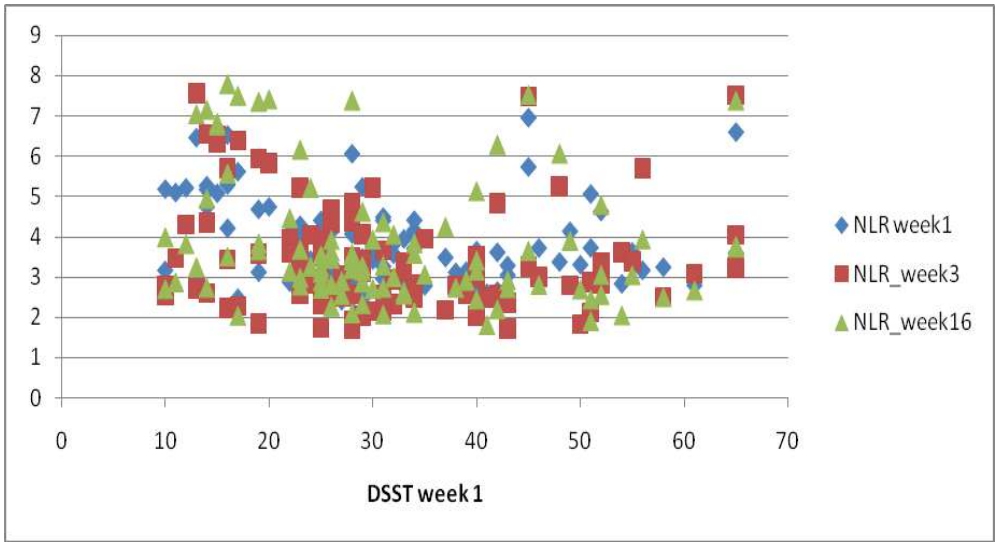

FIGURE NO. 42 (A) CORRELATION OF DSST AT WEEK 1 AND NLR AT WEEKS 1, 3 AND 16

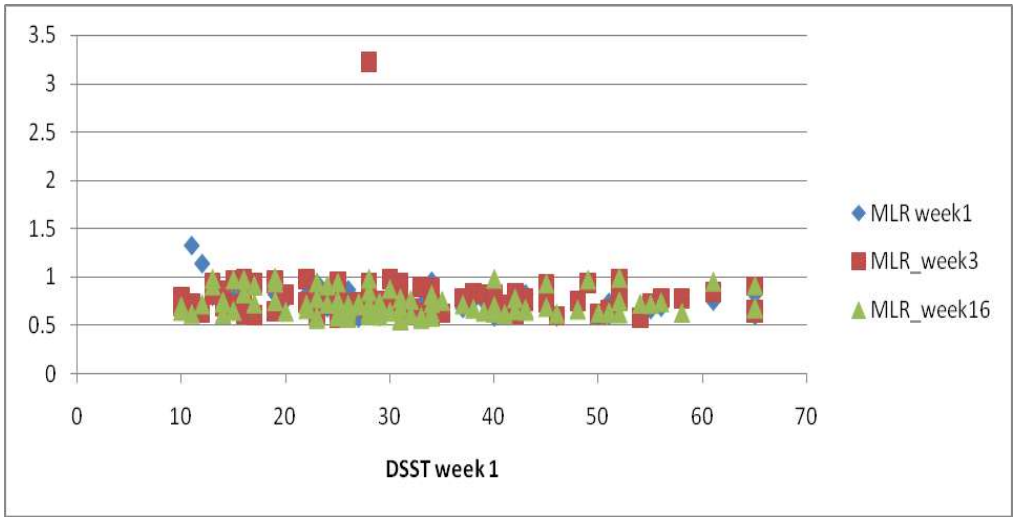

FIGURE NO. 42 (B) CORRELATION OF DSST AT WEEK 1 AND MLR AT WEEKS 1, 3 AND 16

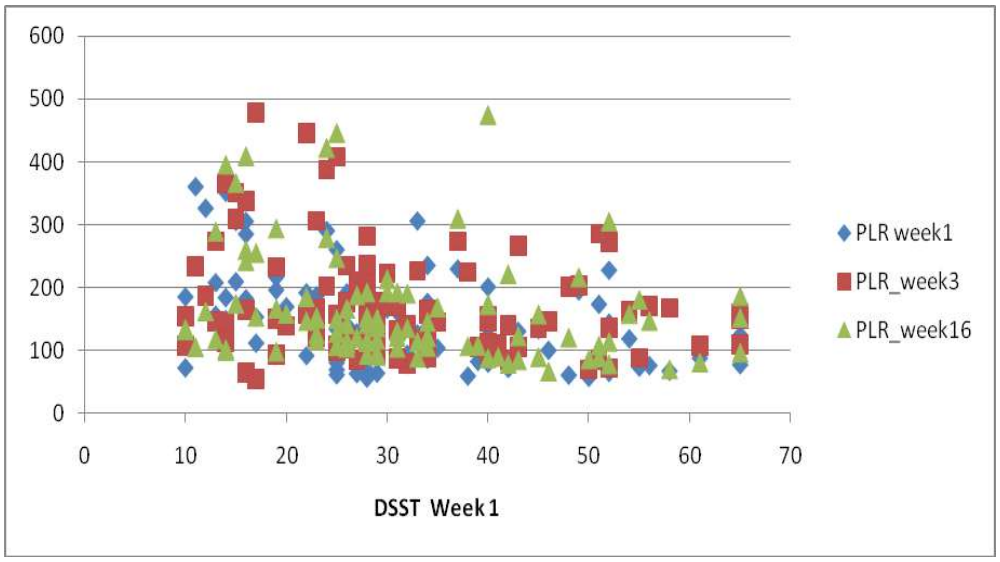

FIGURE NO. 42 (C) CORRELATION OF DSST AT WEEK 1 AND PLR AT WEEKS 1, 3 AND 16

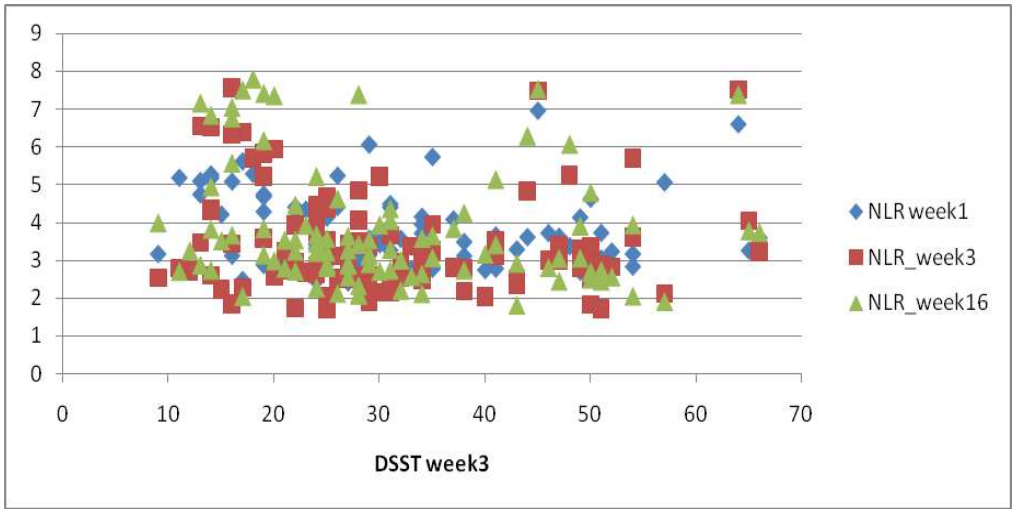

FIGURE NO. 42 (D) CORRELATION OF DSST AT WEEK 3 AND NLR AT WEEKS 1, 3 AND 16

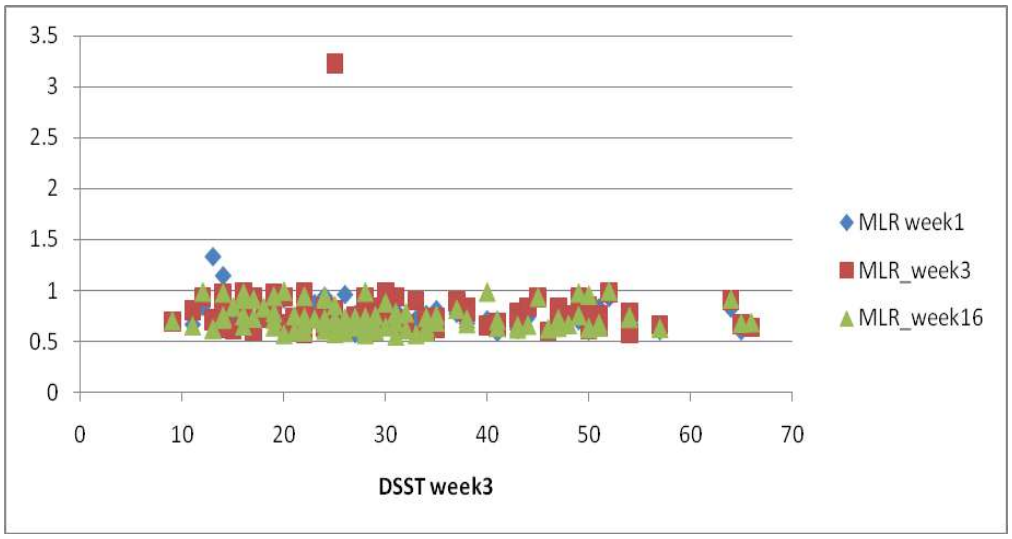

FIGURE NO. 42 (E) CORRELATION OF DSST AT WEEK 3 AND MLR AT WEEK 1, 3 AND 16

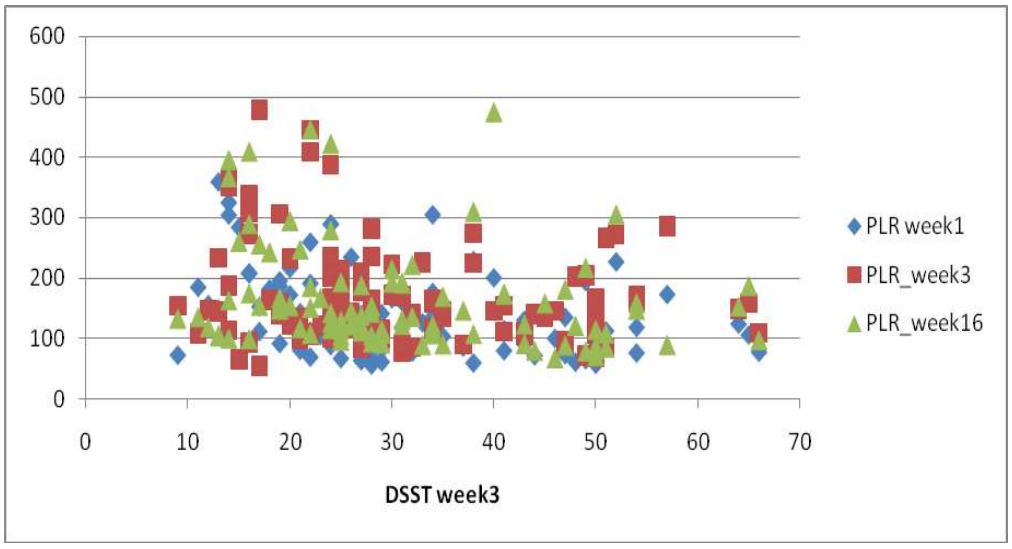

FIGURE NO. 42 (F) CORRELATION OF DSST AT WEEK 3 AND PLR AT WEEK 1, 3 AND 16

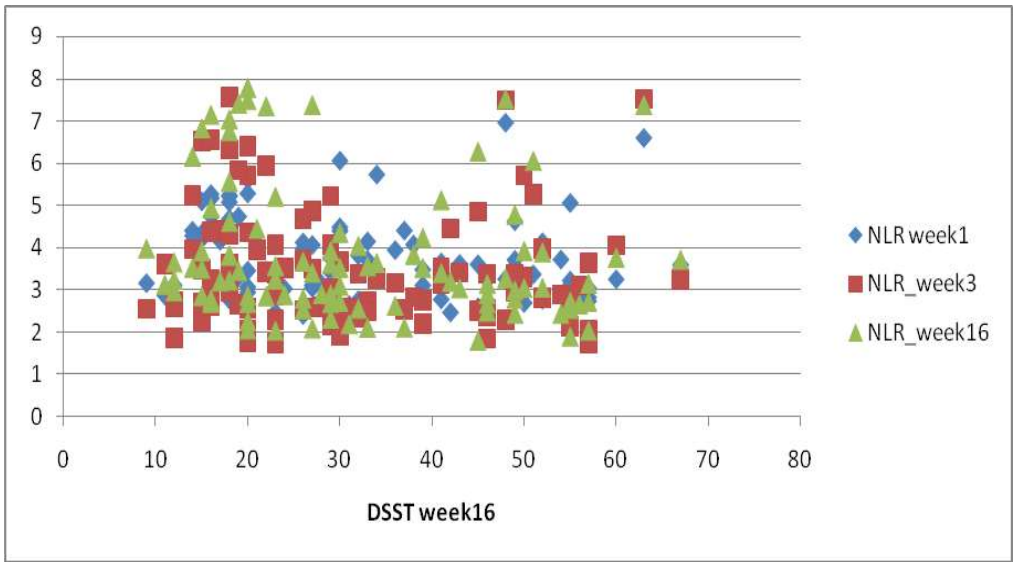

FIGURE NO. 42 (G) CORRELATION OF DSST AT WEEK 16 AND NLR AT WEEK 1, 3 AND 16

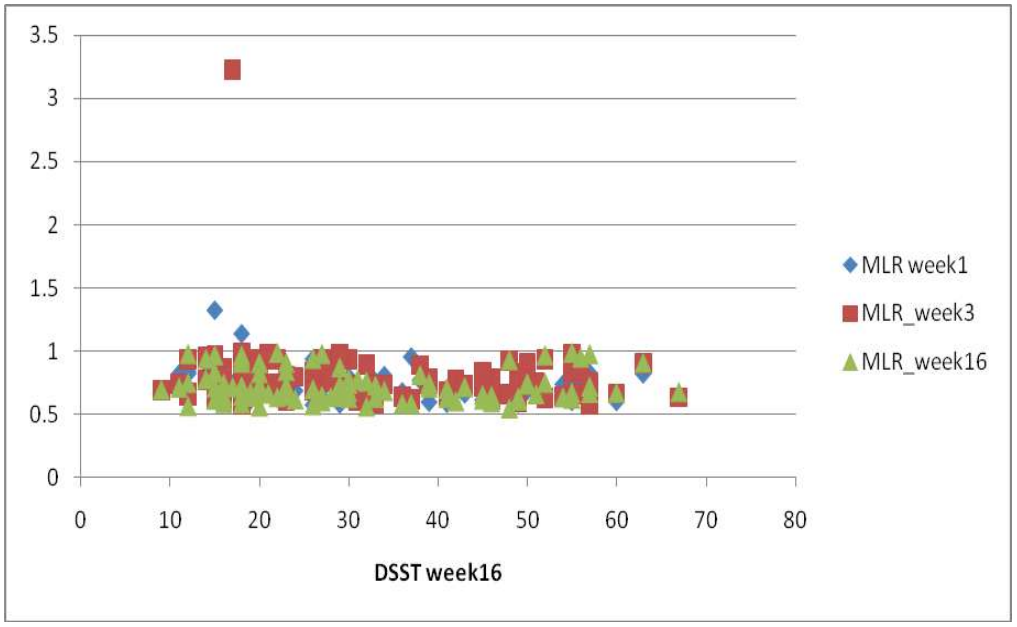

FIGURE NO. 42 (H) CORRELATION OF DSST AT WEEK 16 AND MLR AT WEEK 1, 3 AND 16

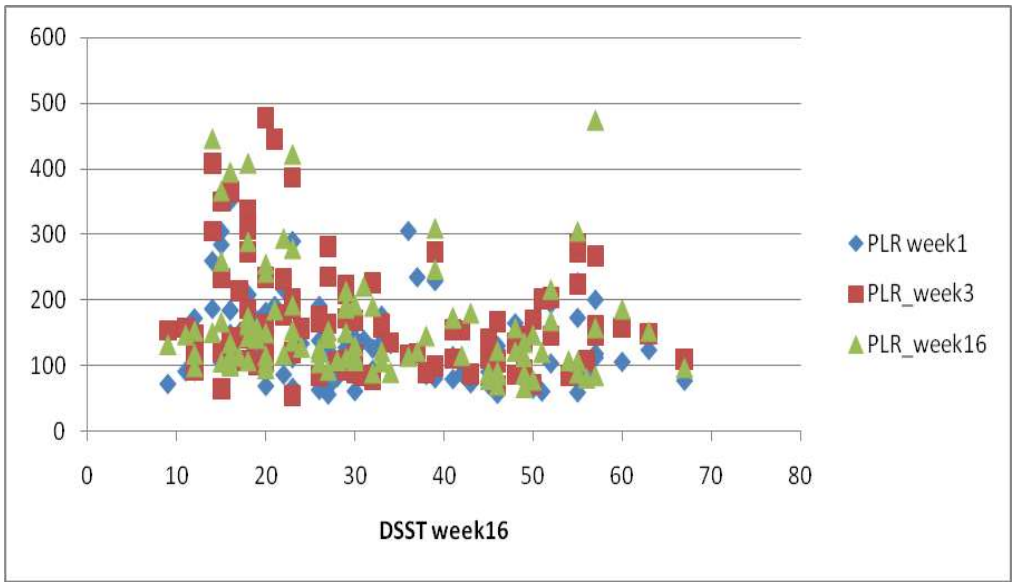

FIGURE NO. 42 (I) CORRELATION OF DSST AT WEEK 16 AND PLR AT WEEK 1, 3 AND 16

; higher levels of inflammatory markers (NLR, MLR, PLR) were significantly associated with lower cognitive performance as measured by the DSST at weeks 1, 3, and 16.

RESULTS

Sociodemographic variables in subjects

Table No.1 and Figure No. 1 present the age distribution among the cases and controls. In the under-30 age group, there were 19 cases, constituting 19.0% of the total cases, while there were 7 controls, making up 23.3% of the total controls. For the 31-40 age group, there were 28 cases (28.0%) and 6 controls (20.0%). In the 41-50 age group, there were 23 cases (23.0%) and 12 controls (40.0%). For those over 50, there were 30 cases (30.0%) and 5 controls (16.7%). In total, there were 100 cases and 30 controls. The chi-square value for this distribution was 4.782, with a p-value of 0.188, indicating no statistically significant age difference between cases and controls.

Table No.2 and Figure No.2 present a comparative analysis of gender distribution between cases and controls, comprising a total sample of 130 participants, including 100 cases and 30 controls. Among the cases, 31% (31 individuals) were female, while 69% (69 individuals) were male. In the control group, 33.3% (10 individuals) were female, and 66.7% (20 individuals) were male. The Chi-square test resulted in a value of 0.058, with a p-value of 0.809, indicating no statistically significant gender difference between cases and controls.

Table No.3 and Figure No.3 show the marital status of the participants. The majority of both the case group (82%) and the control group (80%) were married, indicating a similar distribution of marital status in both groups. Unmarried individuals comprised 18% of cases and 20% of controls. The Chi-square test produced a value of 0.061, with a p-value of 0.804, showing no statistically significant difference in marital status between cases and controls.

Table No.4 and Figure No.4 depict the educational distribution among cases and controls. Graduation was the most common educational level among cases (33%) and controls (30%), followed by matriculation, which accounted for 28% of cases and 13.3% of

controls. Higher secondary education was completed by 16% of cases and 33.3% of controls. Post-graduation was completed by 9% of cases and 16.7% of controls, indicating a higher proportion in the control group. Primary education was reported by 8% of cases and 6.7% of controls, while middle school level was the least common, with 5% of cases and none in the control group. Only one case had a diploma, with no equivalent in the control group. The Chi-square value was 8.66, with a p-value of 0.194, showing no statistically significant difference in educational distribution between cases and controls.

Table No.5 and Figure No.5 display the occupational distribution among the case and control groups. The largest group within the cases was unemployed individuals, constituting 45%, compared to 30% in the control group. Semi-skilled workers made up 27% of cases and 20% of controls. Both professional and semi-professional occupations were equally represented by 11% in both the case and control groups. However, professionals accounted for a higher percentage in the control group at 20%, compared to 11% in the case group. Skilled workers comprised 3% of cases and 10% of controls, and unskilled laborers made up 3% of cases and 6.7% of controls. The Chi-square value for this distribution was 6.49, with a p-value of 0.261, indicating no statistically significant difference in occupational distribution between cases and controls.

Table 6 and Figure No. 6 display the distribution of patients according to family type. Among the 100 cases, 23 (23%) were from joint families, and 77 (77%) were from nuclear families. In the control group of 30 individuals, 7 (23.3%) were from joint families, and 23 (76.7%) were from nuclear families. The chi-square test yielded a value of 0.001 with a p-value of 0.97, indicating no statistically significant difference in the distribution of family types between the case and control groups.

Table 7 and Figure No. 7 present the religious affiliations among cases and controls. Out of 100 cases, 1 was Christian (1%), 42 were Hindu (42%), and 57 were Sikh (57%). In the control group of 30, there

were 1 Christian (3.3%), 19 Hindus (63.3%), and 10 Sikhs (33.3%). Overall, there were 130 participants, with Christians being the least represented. The chi-square test resulted in a value of 5.563 with a p-value of 0.062.

Table No. 8 and Figure No. 8 detail the distribution of cases and controls based on their residence. Among the 100 cases, 43 (43%) resided in rural areas, and 57 (57%) in urban areas. The control group, consisting of 30 individuals, had 13 (43.3%) from rural areas and 17 (56.7%) from urban areas. The total number of participants was 130. The chi-square test resulted in a value of 0.001 with a p-value of 0.974, suggesting no significant difference in the residence distribution between cases and controls.

Table No. 9 and Figure No. 9 show the presence of a family history of bipolar disorder among the 100 cases. It was found that 79 cases (79%) did not have a family history of bipolar disorder, while 21 cases (21%) did. This indicates that the majority of the cases did not have a known family history of bipolar disorder.

Table No.10 and Figure No. 10 show the type of mood stabilizers the patients were taking (N=100). It indicates that 56 cases (56%) were on lithium, while 44 cases (44%) were on sodium valproate.

Table No.11 and Figures No. 11(a) and 11(b) present the mean age and income of the cases and controls. The mean age of the cases was 43 years with a standard deviation (SD) of 13, while the controls had a mean age of 41 years with an SD of 10.57. The Z-score for age was 0.789, with a p-value of 0.443, indicating no significant age difference between the two groups. Similarly, the mean income for the cases was Rs.56,096 with an SD of Rs.65,126.96, while the controls had a mean income of Rs.54,966.33 with an SD of Rs.44,949.12. The Z-score for income was -0.589, with a p-value of 0.556, also indicating no significant difference in income.

Table No. 12 and Figure No. 12 detail the duration of illness among the 100 cases, categorized into three groups: less than 5 years, between 5 to 10 years, and more than 10 years. The results show that 39 cases (39%) had an illness duration of less than 5 years, 21 cases (21%) had an illness duration between 5 to 10 years, and 40 cases (40%) had an illness duration of more than 10 years. The mean duration of illness was reported to be 10 years, with a standard deviation of 12.6 years.

Cognition in subjects

Table No. 13 and Figure No. 13 compare cognitive scores at baseline (week 1) between cases and controls, showing that cases had significantly lower mean scores across several parameters. Cases exhibited deficits in recent memory (mean 4.74, SD 0.48) compared to controls (mean 5.00, SD 0.37) (p=0.009), attention and concentration (mean 9.20, SD 1.69) vs. controls (mean 12.03, SD 1.61) (p=0.001), delayed recall (mean 8.64, SD 1.43) vs. controls (mean 9.63, SD 0.49) (p=0.001), immediate recall (mean 10.96, SD 1.14) vs. controls (mean 11.77, SD 0.63) (p=0.001), visual retention (mean 10.51, SD 2.06) vs. controls (mean 12.07, SD 0.94) (p=0.001), and recognition (mean 8.64, SD 1.11) vs. controls (mean 9.57, SD 0.63) (p=0.001).

Table No. 14 and Figure No. 14 present cognitive function assessments at 3 weeks. Recent memory scores were lower in cases (mean 4.72, SD 0.49) compared to controls (mean 4.93, SD 0.25) (p=0.020). Attention and concentration scores were significantly lower in cases (mean 8.79, SD 1.76) than in controls (mean 11.97, SD 1.47) (p=0.001). Cases also showed weaker delayed recall (mean 8.30, SD 1.54) compared to controls (mean 9.70, SD 0.47) (p=0.001). Immediate recall scores were lower in cases (mean 10.89, SD 1.29) than in controls (mean 11.93, SD 0.74) (p=0.001). Visual retention was lower in cases (mean 10.75, SD 2.00) versus controls (mean 12.27, SD 0.74) (p=0.001). Recognition scores were also poorer in cases (mean 8.67, SD 1.19) compared to controls (mean 9.70, SD 0.47) (p=0.001).

Overall, cases demonstrated significant cognitive deficits in recent memory, attention and concentration, delayed recall, immediate recall, visual retention, and recognition compared to controls.

Table No. 15 and Figure No. 15 compare cognitive function between cases and controls at 16 weeks, again showing significant cognitive deficits in cases. Recent memory scores were lower in cases (mean 4.76, SD 0.59) compared to controls (mean 4.93, SD 0.25) (p=0.034). Attention and concentration scores were significantly lower in cases (mean 8.38, SD 1.33) versus controls (mean 12.07, SD 1.26) (p=0.001). Delayed recall was poorer in cases (mean 7.93, SD 1.63) compared to controls (mean 9.83, SD 0.38) (p=0.001). Immediate recall scores were lower in cases (mean 10.55, SD 1.28) than in controls (mean 12.13, SD 0.57) (p=0.001). Visual retention scores were significantly lower in cases (mean 10.07, SD 2.39) compared to controls (mean 12.23, SD 0.68) (p=0.001). Recognition scores were also poorer in cases (mean 8.57, SD 1.22) compared to controls (mean 9.87, SD 0.35) (p=0.001). Overall, at 16 weeks, cases continued to exhibit significant cognitive deficits in recent memory, attention and concentration, delayed recall, immediate recall, visual retention, and recognition compared to controls.

Table 16 and Figure 16 illustrate the total score of memory at weeks 1, 3, and 16, as well as change from baseline to weeks 3 and 16 for both cases and controls. Cases had significantly lower mean scores at week 1 (mean 82.08, SD 11.47), week 3 (mean 81.59, SD 12.07), and week 16 (mean 79.18, SD 12.37) compared to controls (week 1: mean 92.90, SD 3.16; week 3: mean 93.90, SD 3.03; week 16: mean 94.10, SD 3.04) (all p=0.001). The mean change in total score of memory from baseline to week 3 was 0.49 (SD 2.42) for cases and -1.00 (SD 1.80) for controls (p=0.001). From baseline to week 16, the mean change was 2.90 (SD 4.66) for cases and -1.20 (SD 3.39) for controls (p=0.001), indicating significant differences. Cases consistently

exhibited significantly lower total score of memory and less decline over time compared to controls.

Table No. 17 and Figure No. 17 present Digit Symbol Substitution Test (DSST) scores for cases and controls, showing significant differences at weeks 1, 3, and 16. Cases had lower DSST scores (week 1: mean 33.18, SD 12.17; week 3: mean 31.84, SD 12.19; week 16: mean 32.81, SD 14.44) compared to controls (week 1: mean 79.60, SD 9.51; week 3: mean 80.10, SD 9.22; week 16: mean 80.17, SD 9.17) (all p=0.001). The mean change from baseline to week 3 was 1.34 (SD 2.66) for cases and -0.50 (SD 0.97) for controls (p=0.001), indicating a significant difference.

Table No. 18 and Figure No. 18 display Trail Making Test A (TMT A) duration, with cases taking significantly longer than controls at week 1 (cases: mean 75.04, SD 56.08; controls: mean 31.03, SD 7.29, p<0.001), week 3 (cases: mean 82.62, SD 75.43; controls: mean 30.67, SD 6.48, p<0.001), and week 16 (cases: mean 84.15, SD 92.30; controls: mean 30.47, SD 6.85, p=0.002), indicating greater difficulty in cognitive processing speed and attention among the cases.

Table 19 and Figure 19 present Trail Making Test B (TMT B) duration and changes over 16 weeks. At week 1, cases had a mean duration of 125.88 (SD 86.28) compared to 63.87 (SD 25.94) for controls (p=0.001). At week 3, cases had a mean duration of 113.77 (SD 74.66) compared to 63.13 (SD 24.36) for controls (p=0.001). At week 16, cases had a mean duration of 108.19 (SD 69.34) compared to 63.10 (SD 23.83) for controls (p=0.001). The change in TMT B duration from week 1 to week 3 showed a mean difference of 12.11 (SD 28.05) for cases and 0.73 (SD 3.68) for controls (p=0.001). From week 1 to week 16, the mean difference was 17.69 (SD 34.02) for cases and 0.77 (SD 3.49) for controls (p=0.001), indicating significant differences. These results suggest that cases experienced greater difficulty with tasks requiring cognitive flexibility and executive function compared to controls.

Markers of inflammation in subjects

Table No. 20 and Figure No. 20 illustrate inflammatory markers at week 1. The Neutrophil to Lymphocyte Ratio (NLR) was 3.82 (SD = 1.09) for cases and 1.95 (SD = 0.86) for controls, with a significant p-value of 0.000. The Monocyte to monocyte-to-lymphocyte ratio (MLR) was 0.74 (SD = 0.13) for cases and 0.22 (SD = 0.13) for controls, also with a significant p-value of <0.001. These results indicate that cases had significantly higher inflammatory markers at week 1 compared to controls.

Table No. 21 and Figure No. 21 present inflammatory markers at 3 weeks. The NLR for cases was 3.48 (SD = 1.36) and 1.71 (SD = 0.85) for controls, with a significant p-value of 0.000. The MLR was 0.79 (SD = 0.27) for cases and 0.19 (SD = 0.10) for controls, with a significant p-value of 0.000. The Platelet to the platelet-to-lymphocyte ratio (PLR) was 169.23 (SD = 85.38) for cases and 126.15 (SD = 61.06) for controls, with a significant p-value of 0.005. These elevated ratios suggest ongoing systemic inflammation in the cases.

Table No. 22 and Figure No. 22 show inflammatory markers at 16 weeks. The NLR was 3.75 (SD = 1.54) for cases and 1.61 (SD = 0.71) for controls, with a significant p-value of 0.000. The MLR was 0.73 (SD = 0.12) for cases and 0.18 (SD = 0.11) for controls, with a significant p-value of 0.000. The PLR was 161.73 (SD = 84.91) for cases and 125.45 (SD = 61.02) for controls, with a significant p-value of 0.016.

Table No. 23 and Figure No. 23 display changes in inflammatory ratios from week 1 to week 3. The change in MLR was -0.05 (SD = 0.28) for cases and 0.02 (SD = 0.06) for controls, with a significant p-value of 0.001. The change in PLR was -24.77 (SD = 81.34) for cases and -0.02 (SD = 4.63) for controls, with a significant p-value of 0.033. This indicates that at 3 weeks, cases continued to show a significant increase in inflammatory markers from the baseline and as compared to controls.

Table No. 24 and Figure No. 24 show no significant changes in inflammatory ratios over 16 weeks for NLR, MLR, and PLR between cases and controls.

Comparison of Cognitive Test Performances, inflammatory markers, and mood stabilizers

Table 25 and Figure 25 illustrate the effects of sodium valproate and lithium on haematological ratios. By the third week, the lithium group had higher NLR, MLR, and PLR compared to the sodium valproate group, with significant p-values of 0.008, 0.001, and 0.014, respectively. This pattern persisted at week 16, with the lithium group continuing to show elevated NLR, MLR, and PLR values compared to the sodium valproate group, as indicated by p-values of 0.001, 0.004, and 0.001, respectively. From baseline to week 16, the lithium group experienced an increase in NLR (p=0.000), MLR, and PLR, whereas the sodium valproate group showed a decrease, with p-values of 0.000, 0.017, and 0.007, respectively.

Table No. 26 and Figure No. 26 present a comparison of TMTA andTMT B durations between patients treated with sodium valproate and lithium. For both TMT A and TMT B, no significant differences were observed between the two groups at weeks 1, 3, or week 16, nor in the changes from week 1 to week 3 and from baseline to week 16.

Table No. 27 and Figure No. 27 compare the total score of memory between patients treated with sodium valproate and lithium. At week 1, the sodium valproate group had a mean score of 82.16 (SD 12.48), while the lithium group had a mean score of 87.96 (SD 11.06), with a significant p-value of 0.016. At week 3, the sodium valproate group had a mean score of 81.68 (SD 13.54), and the lithium group had a mean score of 87.55 (SD 11.29), with a significant p-value of 0.020. The change in the total score of memory from baseline to week 16 showed a mean change of 1.61 (SD 5.31) for the sodium valproate group and 4.29 (SD 4.96) for the lithium group, with a significant p-value of 0.011. The sodium valproate group had a significantly lower total score of

memory than the lithium group at week 1 and week 16, with a significantly greater decline in total memory scores over 16 weeks observed in the lithium group compared to the valproate group.

Table No. 28 and Figure No. 28 compare Digit Symbol Substitution Test (DSST) scores between patients treated with sodium valproate and lithium. No significant differences in scores were found between patients treated with sodium valproate and lithium at any time point, nor in changes from baseline.

Comparison of cognitive test outcomes, inflammatory markers, and mood stabilizers.

Table No. 29 and Figure No. 29 present a comparative analysis of Trail Making Test (TMT) A and B scores between female and male participants. For both TMT A and TMT B, no significant differences were observed at week 1, week 3, or week 16, nor in changes from week 1 to week 3 and from baseline to week 16.

Table No. 30 and Figure No. 30 compare the total score of memory between female and male participants. No significant differences in total score of memory were found at week 1, week 3, or week 16, nor in changes from week 1 to week 3 and from baseline to week 16.

Table 31 and Figure No. 31 compare Digit Symbol Substitution Test (DSST) scores between female and male participants. No significant differences in DSST scores were found at weeks 1, 3, or week 16, nor in the changes from baseline to week 3 and from baseline to week 16.

Table 32 and Figure No. 32 compare the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR) between female and male participants at various time points. At week 1, PLR was significantly higher in females (mean 170.82, SD 81.89) compared to males (mean 132.61, SD 63.66) ($p=0.013$). At week 3, PLR remained significantly higher in females (mean 202.38, SD 83.01) compared to males (mean 154.33, SD 82.74)

(p=0.009). At 16 weeks, NLR was significantly higher in females (mean 4.33, SD 1.77) compared to males (mean 3.48, SD 1.35) (p=0.010); MLR was higher in females (mean 0.78, SD 0.13) compared to males (mean 0.70, SD 0.11) (p=0.004); and PLR was higher in females (mean 211.29, SD 112.84) compared to males (mean 139.47, SD 57.07) (p<0.001). From baseline to 16 weeks, the change in NLR was significant, with females showing a mean change of -0.29 (SD 1.30) and males 0.24 (SD 1.10) (p=0.040); the change in MLR was significant, with females at -0.04 (SD 0.11) and males at 0.04 (SD 0.14) (p=0.005); and the change in PLR was significant, with females at -40.47 (SD 75.18) and males at -6.86 (SD 68.73) (p=0.030). These findings suggest that females consistently exhibited higher levels of inflammatory markers (NLR, MLR, PLR) compared to males at several time points, indicating a stronger inflammatory response. Additionally, significant increase in these markers was observed from baseline to 16 weeks in females.

Comparison of cognitive test outcomes, levels of inflammatory markers, and the duration of illness.

Table 33 and Figure No. 33 present data on the duration of illness and Trail Making Test (TMT A and TMT B) durations across three groups based on illness duration: less than 5 years, 5-10 years, and greater than 10 years. For TMT A, significant differences were found at week 1 (p=0.003), week 3 (p<0.001), and 16 weeks (p<0.001). Significant changes in TMT A duration were also observed from baseline to week 3 (p<0.001) and from baseline to 16 weeks (p<0.001). For TMT B, no significant differences were observed at any time point or in the changes from baseline, suggesting that the duration of illness influenced simpler cognitive tasks (TMT A) but not more complex tasks (TMT B).

Table 34 and Figure No. 34 outline the total score of memory across different durations of illness (< 5 years, 5-10 years, > 10 years). No significant differences were found in the total score of memory at

weeks 1, 3, and 16. Additionally, there were no significant changes in total score of memory from week 1 to week 3 and from week 1 to week 16.

Table 35 and Figure No. 35 provide data on the Digit Symbol Substitution Test (DSST) performance across different durations of illness (< 5 years, 5-10 years, > 10 years). Significant differences were observed in DSST scores at week 1 ($p<0.001$), week 3 ($p<0.001$), and 16 weeks ($p<0.001$). However, no significant differences were found in the changes from baseline to weeks 3 and 16.

Table 36 and Figure No. 36 present data on various leukocyte ratios (NLR, MLR, PLR) across different durations of illness (< 5 years, 5-10 years, > 10 years). At week 1, significant differences were found in NLR ($p<0.001$), MLR ($p<0.001$), and PLR ($p<0.001$). At week 3, significant differences were observed in NLR ($p=0.004$) and PLR ($p<0.001$). At 16 weeks, significant differences were found in NLR ($p=0.004$), MLR ($p=0.002$), and PLR ($p=0.003$). The duration of illness significantly impacted leukocyte ratios (NLR, MLR, PLR) at weeks 1, 3, and 16 but did not significantly affect the changes in these ratios over time.

Correlations between age, illness duration, cognitive function, and inflammatory markers.

Table 37 (A-B) and Figure No. 37 (A-F) show Spearman's rho correlations between cognitive performance measures and two key variables: age and duration of illness. Significant positive correlations with age were found for TMT A duration at weeks 1,3 and 16 ($p=0.003,<0.001,<0.001$ respectively), and TMT B duration at weeks 1,3, and 16 ($p=<0.001$ for all). Negative correlations were observed with the total score of memory at week 1 ($p=0.001$), week 3 ($p=0.002$), and 16 weeks ($p=0.014$). The duration of illness showed strong positive correlations with TMT A and TMT B duration at week 1 ($p<0.001$), TMT A and TMT B duration at week 3 ($p<0.001$), and TMT A and TMT B

duration at 16 weeks ($p<0.001$), and significant negative correlations for changes in TMT A duration from week 1 to week 16 ($p=0.002$). Additionally, the duration of illness had strong negative correlations with DSST scores at weeks 1, 3, and 16 ($p<0.001$ for all).

Table 38 (A-B) and Figure No. 38 (A-C) show Spearman's rho correlations between inflammatory markers and age, indicating that age was not significantly correlated with any inflammatory ratios. However, the duration of illness exhibited significant positive correlations with several inflammatory markers, including PLR at week 1 ($p<0.001$), NLR at week 1 ($p=0.001$), MLR at week 1 ($p=0.002$), NLR at week 3 ($p=0.003$), MLR at week 3 ($p=0.011$), and PLR at week 3 ($p=0.005$).

Table 39 (A-B) and Figure No. 39 (A to J) show Spearman's rho correlations between TMT A duration and inflammatory markers. TMT A duration at week 1 had positive correlations with NLR ($p=0.035$) and PLR ($p=0.014$) at week 1. TMT A at 3 weeks was positively correlated with NLR ($p=0.016$), MLR ($p=0.032$), and PLR ($p=0.005$) at week 1, and PLR at week 3 ($p=0.024$). Changes in TMT A duration from week 1 to 16 weeks had positive correlations with NLR ($p=0.007$) and PLR ($p=0.009$) at week 1, and MLR at week 3 ($p=0.026$). Negative correlations were observed for changes in TMT A from baseline to 3 weeks with NLR ($p<0.001$) and PLR ($p<0.001$) at week 1, and PLR at week 3 ($p=0.026$). Changes in TMT A from baseline to 16 weeks showed negative correlations with NLR ($p<0.001$) and PLR ($p<0.001$) at week 1, NLR at week 3 ($p=0.002$), and PLR at week 16 ($p<0.001$).

Table 40 (A-B) and Figure No. 40 (A-C) show the Spearman's rho correlations between various inflammatory markers (NLR, MLR, and PLR) and Trail Making Test B (TMT B) duration weeks 3 and 16. A weak positive correlation was found between the change in TMT B duration from baseline to week 3 and the change in MLR from baseline to week 16 ($r=0.217$, $p=0.030$) and between the change in TMT B

duration from baseline to week 16 and the change in PLR from baseline to week 16 (r=0.266, p=0.007).

Table 41 (A-B) and Figure No. 41 (A-D) show Spearman's rho correlations between inflammatory markers and total score of memory. NLR at week 16 had a significant positive correlation with the total score of memory at week 16 (p=0.029). Changes in the total score of memory at 16 weeks had significant positive correlations with NLR at week 3 (p=0.004) and MLR at week 3 (p=0.034), and with NLR at week 16 (p=0.008). Significant negative correlations were observed between changes in the total score of memory at 16 weeks NLR at week 3 (p=0.009), and NLR at week 16 (p=0.003). Additionally, there were near-significant positive correlations for NLR with the change in the total score of memory at 3 weeks (p=0.053) and near-significant negative correlations for NLR with change in the total score of memory at 3 weeks (p=0.058) and 16 weeks (p=0.090).

Table 42 (A-B) and Figure No. 42 (A-J) show significant negative correlations between inflammatory markers and DSST scores. For DSST at week 1, NLR, MLR, and PLR had significant negative correlations with p-values of 0.026, 0.012, and 0.000, respectively. At week 3, PLR had a significant negative correlation with DSST (p=0.034). At week 16, NLR and PLR had significant negative correlations with DSST (p=0.007 and 0.003, respectively). For DSST at 3 weeks, NLR, MLR, and PLR at week 1 had significant negative correlations with p-values of 0.037, 0.008, and 0.000, respectively. At week 16, NLR and PLR had significant negative correlations with DSST (p=0.011 and 0.004, respectively). For DSST at 16 weeks, NLR, MLR, and PLR at week 1 had significant negative correlations with p-values of 0.030, 0.006, and 0.000, respectively. At week 16, NLR and PLR had significant negative correlations with DSST (p=0.025 and 0.024, respectively). Changes in DSST from week 1 to week 3 had significant negative correlations with NLR and PLR at week 1 (p=0.028

nd 0.036, respectively). This suggests that inflammation, as indicated by these markers, negatively impacts cognitive performance over time.

DISCUSSION

Bipolar disorder is a chronic psychiatric condition characterized by alternating mood states of (hypo)mania and depression, significantly affecting cognitive functions like memory, attention, and executive function, even during periods of mood stability. These cognitive impairments can impact daily activities, work performance, and overall quality of life, making it crucial to address them for comprehensive treatment and better patient outcomes. Research has explored cognitive deficits in euthymic BD patients and their first-degree relatives at risk, often reinforcing the idea that these deficits may act as possible trait markers for BD.[104-110].

Elevated levels of inflammatory markers in individuals with bipolar disorder suggest a link between inflammation and both mood dysregulation and cognitive impairment. The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR) are increasingly recognized as valuable, feasible, and reliable markers of inflammation. These ratios, derived from routine complete blood count (CBC) tests, do not incur additional costs, making them a cost-effective alternative to more expensive specific tests. Understanding these markers can shed light on the impact of inflammation on the disorder's pathophysiology, potentially aiding in assessing disease activity and therapeutic effectiveness.

A study by Goyal et al. [111] examined inflammatory markers in bipolar disorder patients. The findings supported the inflammatory pathophysiology of mania, evidenced by significantly higher neutrophil counts and NLR, and significantly lower lymphocyte counts in both first-episode and bipolar mania patients compared to healthy controls. Despite some existing research, the integration of cognition and inflammation in bipolar disorder remains underexplored in India.

In our study, we assessed cognitive function and evaluated inflammatory markers, including NLR, MLR, and PLR, in 100 patients

with bipolar disorder and compared them to a control group of 30 participants. The assessment was conducted over 16 weeks, with follow-ups at weeks 1, 3, and 16. Cognitive functionswere measured using the PGI Memory Scale, the Digit Symbol Substitution Test, and the Trail Making Test A and B.

In our study, the mean age of participants with bipolar disorder was 43 ± 13 years, while the control group had a mean age of 41 ± 10.57 years. The predominant age group for cases was 31-40 years, representing 28% of participants, whereas for controls, it was the 41-50 years age group, comprising 40%. This is consistent with findings from Dhiman S. et al. (2022) [112], who reported a mean age of 42.31 ± 12.12 years, and Grover S. et al. (2023) [113], who found a mean age of 45.66 ± 10.5 years for bipolar patients. Females constituted 31% of cases and 33.3% of controls, with males making up 69% and 66.7%, respectively, showing no significant gender differences between cases and controls, similar to results from Grant et al. (2009) [114].

Regarding marital status, 82% of both cases and controls were married, aligning with findings from Verma et al. (2016) [115] and Grover S. et al. (2023) [113], who noted similar marital trends among bipolar patients. In terms of education, graduation was the most common educational attainment, observed in 33% of cases and 30% of controls, which may contribute to a better prognosis. This parallels the findings of Reddy MS et al. (2022) [116], where 44.9% of patients were graduates, indicating no significant educational differences, similar to observations by Craddock and Jones (1999) [117] and El Safy, E.R. (2020) [118].

In our study, the largest subgroup among bipolar disorder cases consisted of unemployed individuals, representing 45%, compared to 30% among controls. This differs from studies by Reddy MS et al. (2022) [116] and Dhiman S. et al. (2022) [112], where most patients were employed. This variance can be attributed to the severity of bipolar symptoms impairing cognitive function and workplace performance,

variations in social and economic support systems across regions, and demographic and methodological differences that influence employment statistics. Our study indicated no notable differences in family types between cases and controls, with 23% from both groups coming from joint families, and 77% of cases and 76.7% of controls from nuclear families, aligning with findings by Gershon et al. (1982) [119] and Dhiman S. et al. (2022) [112].

Geographically, 43% of both cases and controls resided in rural areas, and 57% resided in urban areas. In contrast, Dhiman S. et al. (2022) [112] and Grover S. et al. (2023) [113] had a majority of their patients from rural areas. Regarding religion, 57% of cases were Sikh and 63.3% of controls were Hindu, highlighting significant differences in religious affiliations. Grover et al. (2016) [120]also reported that most of the patients in their study were of Hindu faith, followed by a considerable number of Sikh patients, with smaller representations from Muslim and Christian communities.

In our study, 79% of individuals with bipolar disorder did not have a familial history of the condition, while 21% did. This closely mirrors findings from Gershon et al. (1982) [119], where 20-25% of bipolar patients reported having a first-degree relative with the disorder, and Craddock and Jones et al. (1999) [117], who identified a familial history in 15-20% of cases. Regarding mood stabilizers, 56% of our patients were on lithium, and 44% were on sodium valproate. Similarly, lithium (64.3%) and valproate (43.2%) were the most frequently prescribed mood stabilizers in a study by Reddy MS et al. (2021) [121].

Our study revealed no significant differences in income between cases and controls, with the average income reported as Rs.56,096 (SD = Rs.65,126.96) for cases and Rs.54,966.33 (SD = Rs.44,949.12) for controls, suggesting that socioeconomic status was not a differentiating factor. Regarding the duration of illness, 39% of cases experienced symptoms for less than 5 years, 21% for 5-10 years, and 40% for more than 10 years, with a mean duration of 10 years (SD = 12.6 years).

This pattern aligns with findings from Swaroopachary RS et al. (2018) [122], who also observed that a significant number of patients with bipolar disorder had an illness duration exceeding 10 years, highlighting the chronic nature of the disorder and its prolonged impact on patients.

Over the past decade, the importance of identifying and addressing cognitive impairments in bipolar disorder (BD), which persist even during remission periods, has been increasingly recognized. Studies indicate that attention impairment in BD is linked to genetic factors such as the CHRNA7 and ALDH2 genes and altered brain metabolism [123]. This is further complicated by structural damage to white matter fiber bundles, impairing attention and cognitive functions. Additionally, reduced metabolic activity in the hippocampus and temporal lobe has been linked with sustained attention deficits [124],Brain volume reduction through cell apoptosiscontributes to cognitive impairments, evident in BD patients' difficulties with short-term memory and verbal fluency [73]. Specific single nucleotide polymorphisms (SNPs) in genes such as CACNA1C, CHRNA7, and MAPK1 are associated with memory impairment in these patients pointing towards genetic matrix involvement.[125].

The cognitive landscape in BD is influenced by serum lipid peroxide (LPH) levels, which negatively correlate with executive function and may be modulated by brain-derived neurotrophic factor (BDNF). During stable periods, decreased BDNF levels are linked to worsened executive performance in BD patients [126,127]. Genetic elements like the MsrA gene and rs4840463 polymorphism have also been implicated in executive function deficits [128]. Neurobiological models suggest that these cognitive impairments involve the frontotemporal lobe and subcortical circuitry [109]. Moreover, the activation of microglia and pathological changes in astrocytes and oligodendrocytes contribute to cognitive deficits. Elevated inflammatory markers such as sTNF-R1, IL-1Ra, and sCD40L are associated with poorer cognitive function in BD

patients, with research indicating that increased levels of interleukin-6, interleukin-10, and CCL24 in BD patients and their siblings suggest an inflammatory basis for these cognitive impairments [129]. Additionally, elevated homocysteine levels have been linked to cognitive deficits in euthymic BD patients [130] and the prevalence of insulin resistance in over half of BD patients is linked with chronic illness, treatment resistance, cognitive impairment, and poor functional outcomes [131].

In our study, cognitive performance was evaluated through the PGI Memory Scale at weeks 1, 3, and 16, showing that individuals with bipolar disorder consistently exhibited significantly lower cognitive scores compared to the control group across various parameters. For Remote Memory, the scores were nearly identical across all assessments, with cases recording mean scores of 5.67, 5.66, and 5.57 at weeks 1, 3, and 16, respectively, while controls consistently scored a mean of 5.70. In Recent Memory, cases scored means of 4.74, 4.72, and 4.76 in the same weeks, compared to controls who scored 5.00, 4.93, and 4.93, indicating slight but statistically significant differences (p=0.009, p=0.020, p=0.034). Attention and Concentration revealed marked disparities, with cases scoring means of 9.20, 8.79, and 8.38 across the three-time points, significantly lower than the controls who scored 12.03, 11.97, and 12.07, respectively (p=0.001 for all).

Delayed Recall also showed significant deficits in cases, with mean scores of 8.64, 8.30, and 7.93 compared to controls' scores of 9.63, 9.70, and 9.83 at weeks 1, 3, and 16, respectively (p = 0.001 for all). Immediate Recall scores for cases were 10.96, 10.89, and 10.55, lower than the controls' scores of 11.77, 11.93, and 12.13 (p = 0.001 for all). Similarly, Visual Retention and Recognition were significantly poorer in cases, with Visual Retention scores of 10.51, 10.75, and 10.07 and Recognition scores of 8.64, 8.67, and 8.57 at weeks 1, 3, and 16, respectively. Controls scored 12.07, 12.27, and 12.23 for Visual Retention (p = 0.001 for all) and 9.57, 9.70, and 9.87 for Recognition (p

= 0.001 for all). Deficits in visual retention and recognition suggest issues with visual processing and memory. Retention for Similar Pairs and Dissimilar Pairs did not show significant differences between cases and controls.

In a naturalistic one-year follow-up study, Sagar R. et al. (2018) [67] reported significant impairments in sustained attention, verbal and visual memory, executive functions, and working memory in bipolar patients compared to controls. Similarly, Martinez-Aran et al. (2004) [132] and Arts et al. (2008) [133] found notable deficits in immediate and delayed recall, attention, executive functions, and verbal memory. They also identified moderate impairments in concept shifting, executive control, visual memory, and sustained attention, with smaller effect sizes observed for visuoperception in individuals with bipolar disorder.

Recent research by Grover S. et al. (2023) [113] identified significant cognitive impairments during the euthymic phase in various domains, including verbal learning, long-delay verbal free recall, delayed non-verbal recall, semantics, verbal fluency, verbal interference, set-switching tasks, immediate non-verbal memory, sustained visual vigilance, speeded visual scanning, and executive functions related to problem-solving tasks. Similarly, a study by Trivedi JK et al. (2008) [25] revealed significant deficits in executive functions, with subtle impairments in attention and working memory. In contrast, no significant differences in Remote Memory, Mental Balance, and Retention for Similar and Dissimilar Pairs suggest these cognitive areas may be less affected by bipolar disorder. Remote Memory, dependent on long-term memory consolidation processes mediated by structures like the hippocampus, appears resilient to the episodic fluctuations characteristic of bipolar disorder. Mental Balance, reflecting cognitive stability and coherence, relies on broader neural networks that are less prone to disruption during mood episodes. Likewise, Retention for Similar and Dissimilar Pairs, which involves basic associative memory processes used in recognition and matching

tasks, seems more robust and less influenced by the executive dysfunctions typically seen in bipolar disorder.

The Total score of memory at weeks 1, 3, and 16, and changes from baseline to week 16, demonstrated that cases had significantly lower mean scores at week 1 (mean 82.08, SD 11.47), week 3 (mean 81.59, SD 12.07), and week 16 (mean 79.18, SD 12.37) compared to controls (week 1: mean 92.90, SD 3.16; week 3: mean 93.90, SD 3.03; week 16: mean 94.10, SD 3.04) (all p=0.001). The mean change in total score of memory from baseline to week 3 was 0.49 (SD 2.42) in cases and -1.00 (SD 1.80) in controls (p=0.001). From baseline to week 16, the mean change was 2.90 (SD 4.66) in cases and -1.20 (SD 3.39) in controls (p=0.001). Cases exhibited significant sustained cognitive impairments across multiple domains when compared to controls. The cognitive deficits observed in individuals with bipolar disorder, especially in memory functions, arise from a confluence of structural, neurochemical, and functional abnormalities.

Studies by Martinez-Aran et al. (2004) [132], Robinson et al. (2006) [14], Torres et al. (2011) [134], Bora et al. (2009) [68], Ekman et al. (2020) [135], Bora and Özerdem (2017) [136], Grover S. et al. (2023) [113], and Taj M. et al. (2005) [72] have consistently demonstrated significant cognitive deficits in individuals with bipolar disorder, including impairments in verbal memory, immediate and delayed recall, attention and concentration, visual retention, recognition, and executive functions. Conversely, Sagar R. et al. (2018) [67] observed no drastic deterioration in cognitive functions over a one-year longitudinal study in bipolar disorder patients. Similarly, Santos JL et al. (2014) [64] conducted a study with assessments five years apart and found that cognitive impairments in bipolar disorder patients, except for verbal recall, remained stable over time.

The Digit Symbol Substitution Test (DSST) revealed significant differences in scores between cases and controls at weeks 1, 3, and 16. Specifically, cases recorded lower DSST scores (week 1: mean

33.18, SD 12.17; week 3: mean 31.84, SD 12.19; week 16: mean 32.81, SD 14.44) compared to controls (week 1: mean 79.60, SD 9.51; week 3: mean 80.10, SD 9.22; week 16: mean 80.17, SD 9.17), with all comparisons yielding p-values of 0.001. The mean change from baseline to week 3 was 1.34 (SD 2.66) for cases and -0.50 (SD 0.97) for controls (p=0.001), indicating a significant difference, though no significant changes were observed at week 16. The significant differences in DSST scores reveal that individuals with bipolar disorder had poorer attention, working memory, and processing speed than controls.

Similar patterns have been documented in previous research on bipolar disorder. Torrent et al. (2012) [137], MacQueen and Memedovich (2017) [138], Krabbendam et al. (2005) [139], and Taj M et al. (2005) [72] noted persistent cognitive deficits in bipolar patients, particularly in processing speed, executive functions, attention, and visuomotor speed. The absence of further change after three weeks might be explained by patients becoming more accustomed to the testing process, potentially reducing test-related anxiety or unfamiliarity that might initially impact performance.

Our study found that at baseline, cases took significantly more time to complete Trail Making Test A (TMT A) (Mean = 75.04, SD = 56.08) compared to controls (Mean = 31.03, SD = 7.29). At Week 3, cases (Mean = 82.62, SD = 75.43) still exhibited more duration than the control group (Mean = 30.67, SD = 6.48). By Week 16, the trend persisted, with cases (Mean = 84.15, SD = 92.30) remaining significantly different from controls (Mean = 30.47, SD = 6.85). No significant changes in TMT A duration were observed from baseline to Week 16. Similarly, Lewandowski et al. (2014) [140] observed that bipolar disorder patients had significantly longer TMT A duration, with an average time of 44.5 seconds (SD = 19.1) compared to healthy controls, who averaged 29.2 seconds (SD = 7.3).

Bora et al. (2009) [68], Ganesh UM et al. (2021) [141], and Taj M et al. (2005) [72] also reported significant impairments in psychomotor speed among bipolar disorder patients, with their meta-analysis indicating consistently prolonged TMT A times relative to controls, highlighting the significant and persistent deficits in psychomotor speed among bipolar disorder patients. This demonstrates that individuals with bipolar disorder consistently face challenges with tasks requiring quick visual-motor coordination and attention, reflecting enduring cognitive impairments that can significantly impact daily functioning and overall quality of life. The baseline impairment in processing speed, as measured by TMT A, might have already been at a significant level, leaving limited room for a further measurable decline over the 16 weeks.

Over 16 weeks, cases showed a decrease in the time taken to complete the Trail Making Test Part B (TMT B), yet they consistently underperformed compared to controls, indicating ongoing cognitive deficits. Initially, the mean duration for cases was 125.88 seconds (SD = 86.28) at week 1, which improved to 113.77 seconds (SD = 74.66) by week 3 and further to 108.19 seconds (SD = 69.34) by week 16. In contrast, controls maintained a more consistent performance with mean times of 63.87 seconds (SD = 25.94) at week 1, slightly improving to 63.13 seconds (SD = 24.36) at week 3, and 63.10 seconds (SD = 23.83) at week 16. The changes from week 1 to week 3 showed a mean reduction of 12.11 seconds (SD = 28.05) for cases and only 0.73 seconds (SD = 3.68) for controls; from week 1 to week 16, the reductions were 17.69 seconds (SD = 34.02) for cases and 0.77 seconds (SD = 3.49) for controls, with all p-values registering at 0.001. These results reflect the challenges cases faced with tasks demanding cognitive flexibility and executive function. Repeated exposure to TMT B can lead to improvements in performance due to familiarity with the test procedures, even in individuals with cognitive deficits.

Complementing these findings, Taj M. et al. (2005) [72], Lopez-Jaramillo et al. (2010) [142], and Samamé C. et al. (2014) [143] also reported significant disparities in TMT B duration between bipolar patients and healthy controls, illustrating worse performance in patients. In particular, younger bipolar patients recorded a mean duration of 58.55 seconds (SD = 23.42) compared to 52.79 seconds (SD = 21.09) in young controls, and older patients had an average time of 115.60 seconds (SD = 56.15) compared to 85.87 seconds (SD = 45.67) in older controls, with both age groups showing statistically significant differences, suggesting that cognitive impairments in bipolar disorder are persistent over time.

Immune dysfunction has been suggested as a potential key neurobiological substrate of cognitive impairment in bipolar disorder (BD), as outlined by Barbosa et al., 2014 [144] and Bauer et al., 2014 [40]. Furthermore, over the past several years, inflammation has been repeatedly shown to play an important role in the pathophysiology of mood disorders, supported by findings from McNamara and Lotrich, 2012 [145] and Rosenblat and McIntyre, 2015 [146]. In BD, the exact mechanism behind inflammation-related events remains unclear. However, recent research highlights several key points: (a) The immune response system is activated by macrophages and T lymphocytes, leading to the release of proinflammatory cytokines. These cytokines are involved in reducing the release of neurotransmitters such as noradrenaline and serotonin in the brain, impacting mood and cognitive functions. (b) Additionally, activated microglia in the brain can negatively impact the neuroprotective system, contributing to BD symptoms. This is mediated by proinflammatory cytokines, further complicating the disorder's pathology, as noted by Mayda H. et al., 2024 [147].

Kalelioglu et al. (2015) [148] reported various immune and inflammatory changes in BD patients, including increased acute phase reactants, abnormal inflammatory cytokine levels, and activated lymphocyte

subsets. The Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) serve as cost-effective and easily obtainable markers of peripheral inflammation. An increase in NLR in BD patients is linked to a heightened immune response, with neutrophils, as primary responders in inflammation, showing a higher count relative to lymphocytes, indicating acute inflammation. Similarly, elevated PLR suggests both inflammation and thrombosis, with platelets playing a role in these processes by increasing relative to lymphocytes, indicating a heightened state of inflammatory and prothrombotic activity. Additionally, the Monocyte-to-Lymphocyte Ratio (MLR) is elevated, with monocytes being precursors to macrophages and dendritic cells, crucial in chronic inflammation. Increased MLR reflects ongoing inflammatory processes typical in the pathophysiology of BD (La Verde et al., 2024) [149].

In our study, the changes in inflammatory markers from baseline (Day 1) to Week 16 in cases showed a persistent inflammatory response. At week 1, cases had significantly higher NLR (3.82 vs. 1.95, $p < 0.001$) and MLR (0.74 vs. 0.22, $p < 0.001$). At Week 3, cases maintained significantly higher NLR (3.48 vs. 1.71, $p < 0.001$), MLR (0.79 vs. 0.19, $p < 0.001$), and PLR (169.23 vs. 126.15, $p = 0.005$). By Week 16, the markers remained elevated in cases with NLR (3.75 vs. 1.61, $p < 0.001$), MLR (0.73 vs. 0.18, $p < 0.001$), and PLR (161.73 vs. 125.45, $p = 0.016$). From baseline to Week 3, NLR decreased slightly in cases (0.34 vs. 0.24), MLR increased significantly in cases (-0.05 vs. 0.02, $p = 0.001$), and PLR also increased significantly in cases (-24.77 vs. -0.02, $p = 0.033$). From baseline to Week 16, NLR showed a minor decrease in cases (0.08 vs. 0.35), MLR changed minimally (0.01 vs. 0.03), and PLR continued to increase significantly in cases (-17.28 vs. 0.68).The minor variations in NLR and MLR from baseline to Week 16 indicate that the acute inflammatory response may have slightly decreased, but it did not fully disappear, suggesting a chronic inflammatory condition.

These findings align with studies by Çakır et al. (2015) [71], which found that patients with bipolar disorder had a significantly higher NLR compared to controls (3.04 vs. 1.97, $p < 0.001$) during acute episodes, indicating increased systemic inflammation. Additionally, Mazza MG et al. (2018) [51] reported that individuals with mania had significantly higher NLR and MLR than controls, reinforcing the inflammatory component in bipolar disorder. These findings underscore the role of inflammatory markers like NLR, MLR, and PLR in monitoring the progression and treatment response in bipolar disorder. Furthermore, a retrospective file review by Ozdin and Ozdin (2020) [150] observed significantly higher neutrophil counts and NLR, while Goyal MK et al. (2021) [77] noted significantly lower lymphocyte counts in cases of bipolar disorder.

In our study, most patients were treated with either lithium or sodium valproate. Initially, at baseline, there were no significant differences between the two medications in terms of NLR, MLR, and PLR. However, by Week 3, patients on sodium valproate exhibited significantly lower mean NLR (2.97 vs. 3.88, $p = 0.008$), MLR (0.77 vs. 0.80, $p = 0.001$), and PLR (146.27 vs. 187.26, $p = 0.014$) compared to those on lithium. These differences persisted into Week 16, with sodium valproate showing continued lower values for NLR (3.00 vs. 4.33, $p = 0.001$), MLR (0.67 vs. 0.77, $p = 0.004$), and PLR (125.80 vs. 189.96, $p = 0.001$). Additionally, the changes from baseline to Week 3 and Week 16 revealed distinctive patterns in inflammatory markers for sodium valproate, marked by a decline in NLR at both time points (0.75 and 0.72) compared to lithium, which showed an increase or minimal changes. Significant differences were also observed in MLR and PLR by Week 16 ($p = 0.017$ and $p = 0.007$, respectively).

The study by Berk et al. (2011) [151] suggests that both medications are effective in mitigating inflammation, with sodium valproate potentially exerting a more pronounced effect due to its pharmacological properties. Lithium has been documented to augment the activity of

mitochondrial complexes, thereby boosting cellular energy production and diminishing oxidative stress. In contrast, sodium valproate stabilizes mitochondrial membranes, aiding in cell protection against oxidative damage and reducing inflammation. Conversely, research by Melo et al. (2019) [89] indicates that there is no significant correlation between NLR and PLR values and the use of psychiatric medications, including mood stabilizers like lithium.

Our study showed no notable differences in TMT A and TMT B duration at any time point between the two treatment groups. Balanza-Martinez et al. (2018) [152] also reported no significant differences in cognitive performance, including mental speed and attention, between lithium and sodium valproate-treated patients at various time points, corroborating our findings. This suggests that both treatments have a similar impact on cognitive performance as both modulate neurotransmitter pathways and exert neuroprotective effects, which could lead to similar impacts on cognitive processes such as mental speed and attention.

In our study, at Week 1, lithium-treated patients had significantly higher Total scores of memory (Mean = 87.96, SD = 11.06) in comparison to those treated with sodium valproate (Mean = 82.16, SD = 12.48, p = 0.016). This trend continued in Week 3, with lithium (Mean = 87.55, SD = 11.29) outperforming sodium valproate (Mean = 81.68, SD = 13.54, p = 0.020). By Week 16, although lithium still showed higher scores (Mean = 83.68, SD = 10.94) compared to sodium valproate (Mean = 80.55, SD = 15.11), the difference was not statistically significant.

The change in Total score of memory from baseline to Week 16 was significantly more pronounced for lithium (Mean change = 4.29, SD = 4.96) compared to sodium valproate (Mean change = 1.61, SD = 5.31, p = 0.011), with lithium-treated patients experiencing a greater decline. These findings are consistent with those reported by Lund, Nissen, and Rafaelsen (1982) [153] and Wingo et al. (2009) [154], who observed that lithium treatment was associated with a relative reduction in memory

and perceptual processing abilities, and a decrease in effort compared to attention, productivity, and emotional reactivity. Additionally, lithium was found to cause a delay in information processing rates and was significantly associated with impairments in immediate verbal learning and memory. The pronounced decline in memory scores among lithium-treated patients compared to those treated with sodium valproate is likely due to the neurobiological effects of lithium, particularly its modulation of neurotransmitter pathways and intracellular signaling through effects on enzymes like GSK-3 [155-157]. Alterations in these pathways, which are critical for neurodevelopment and synaptic plasticity, can disrupt memory processing and retrieval, leading to the observed decline in memory performance.

At Week 1, patients treated with lithium had higher DSST scores (Mean = 32.80, SD = 14.76) in comparison to those treated with sodium valproate (Mean = 30.48, SD = 11.61); however, this difference was not statistically significant. This trend continued in Week 3, with lithium showing a mean score of 31.64 (SD = 14.16) versus 29.93 (SD = 12.23) for sodium valproate. By Week 16, the mean scores were 33.36 (SD = 15.26) for lithium and 30.02 (SD = 14.21) for sodium valproate, again with no significant difference. Changes in DSST scores from baseline to Week 3 indicated a mean change of 0.55 (SD = 3.02) for sodium valproate and 1.16 (SD = 3.18) for lithium, and from baseline to Week 16, the mean change was 0.45 (SD = 6.93) for sodium valproate and -0.55 (SD = 7.25) for lithium. Despite a consistent trend of higher DSST scores in lithium-treated patients across all time points, the differences were not statistically significant, suggesting that both medications similarly affect cognitive processing speed and working memory over 16 weeks. These findings align with Mur et al. (2008) [158], who reported stable cognitive impairments in lithium-treated bipolar patients over two years, and Muralidharan et al. (2015) [159], who found no significant differences in processing speed and other cognitive domains between lithium and valproate (all $p > 0.13$).A 16-week timeframe might be insufficient to detect significant differences in

cognitive function between the two treatments. Long term studies may be necessary to identify more pronounced differences.

The comparison of Trail Making Test (TMT) duration between female and male participants in our study showed no significant differences at any time point. At week 1, the mean TMT A duration was 63.95 (SD = 51.01) for females and 63.50 (SD = 45.09) for males (p = 0.965). Similar non-significant results were observed at 3 weeks and 16 weeks, as well as in changes in TMT A and TMT B duration over 16 weeks. A study by Tombaugh et al. (2004) [160] also found no significant gender differences in TMT scores among healthy adults.

Our study observed that females achieved a higher mean total score of memory compared to males at each assessed time point; however, these differences did not reach statistical significance. The mean total score of memory for males was 83.94 (SD = 12.06), 83.46 (SD = 12.91), and 81.25 (SD = 13.76) at Weeks 1, 3, and 16, respectively. For females, the corresponding scores were 88.68 (SD = 11.39), 88.32 (SD = 11.41), and 84.65 (SD = 10.82). The changes in total score of memory from baseline to Week 3 were minor, with males showing a decline of 0.48 (SD = 2.72) and females a decline of 0.35 (SD = 2.78), neither of which was statistically significant. Similarly, the changes from baseline to Week 16 were 2.70 (SD = 5.25) for males and 4.03 (SD = 5.26) for females, also not reaching statistical significance.

Although females consistently had higher total scores of memory than males in our study, the differences were not significant at any time point. In contrast to our study, Lee J. et al. (2014) [161] found significant gender differences in cognition, with females outperforming males, whereas Langa K.M. et al. (2008) [162] reported that males performed better than females in cognitive assessments. These mixed results highlight the complexity of gender differences in cognitive performance. The absence of statistically significant differences in our study may be attributed to the limited sample size, which reduces the statistical

power to detect small yet potentially meaningful differences between genders.

In our study, the Digit Symbol Substitution Test (DSST) scores for males at Weeks 1, 3, and 16 were 32.55 (SD = 12.72), 31.35 (SD = 12.37), and 32.06 (SD = 14.18) respectively. For females, the scores were 30.06 (SD = 15.03), 29.87 (SD = 15.36), and 31.52 (SD = 16.42) at the same time points, and these differences were not significant. The changes in DSST scores from baseline to Week 3 showed a decline of 1.20 (SD = 3.48) for males and 0.19 (SD = 1.96) for females, and from baseline to Week 16, a decline of 0.49 (SD = 7.47) for males and a decrease of 1.45 (SD = 6.09) for females, both of which were also not significant. These findings align with those of Royall et al. (2004) [163], which reported no significant gender differences in DSST performance. Our results suggest that gender does not substantially affect processing speed, attention, working memory, or visual-motor coordination.

In our study, in Week 1, we investigated inflammatory ratios between females and males. The mean NLR was higher in females (4.05 ± 1.23) than in males (3.72 ± 1.02), although this difference was not statistically significant. The MLR was similar between genders (females: 0.73 ± 0.10, males: 0.74 ± 0.14), while the PLR was significantly higher in females (170.82 ± 81.89) compared to males (132.61 ± 63.66, $p = 0.013$). By Week 3, the NLR in females (3.83 ± 1.75) continued to be higher than that in males (3.33 ± 1.12), nearing statistical significance ($p = 0.085$), with no significant difference in MLR. By Week 16, females showed significantly higher NLR (4.33 ± 1.77 vs. 3.48 ± 1.35, $p = 0.010$), MLR (0.78 ± 0.13 vs. 0.70 ± 0.11, $p = 0.004$), and PLR (211.29 ± 112.84 vs. 139.47 ± 57.07, $p < 0.001$) compared to males, underscoring persistent gender disparities in inflammatory responses over time.

We studied the changes in the NLR, MLR, and PLR from baseline to Week 3 and found no statistically significant differences between

genders. However, from baseline to Week 16, there was a notable increase in NLR in females (-0.29 ± 1.30) compared to males (0.24 ± 1.10, p = 0.040). Additionally, MLR showed a significant increase in females (-0.04 ± 0.11) versus an increase in males (0.04 ± 0.14, p = 0.005). PLR also significantly increased in females (-40.47 ± 75.18) compared to males (-6.86 ± 68.73, p = 0.030), indicating a higher and more dynamic inflammatory response in females, particularly regarding platelet involvement. This suggests the need for gender-specific therapeutic strategies to manage potential complications such as cardiovascular diseases. Recognizing these distinct inflammatory patterns can help clinicians tailor treatments more effectively. In contrast, a study by Lee JS et al. (2018) [164] found that men exhibited higher NLR and PLR values, indicating a stronger inflammatory response (NLR, PLR p < 0.001), while MLR showed no significant differences between genders (p = 0.682), underscoring the variability in gender-related inflammatory responses across different studies.

Our study demonstrated that a longer duration of illness in bipolar disorder correlated with greater cognitive decline, as evidenced by deteriorating performance on the Trail Making Test Part A (TMT A). Specifically, patients with an illness duration of less than 5 years exhibited superior performance at Week 1 (Mean = 52.61, SD = 23.93), Week 3 (Mean = 49.92, SD = 23.74), and Week 16 (Mean = 44.61, SD = 23.64) compared to those with an illness duration of 5-10 years or over 10 years, with these differences being statistically significant (F = 6.01, p = 0.003; F = 9.82, p < 0.001; F = 10.12, p < 0.001, respectively). The change in TMT A durations from baseline to Week 3 (Δ TMT A WEEK 3: -24.93, SD = 45.28, p < 0.001) and from baseline to Week 16 (Δ TMT A WEEK 16: -35.55, SD = 70.84, p < 0.001) was statistically significant, further highlighting that patient with an illness duration over 10 years experienced significant performance declines. Conversely, the Trail Making Test Part B (TMT B) did not exhibit significant differences across various illness durations.

Our findings were consistent with those reported by Robinson and Ferrier (2006) [14] and Martínez-Arán et al. (2005) [132], that cognitive impairments in bipolar disorder, including executive function, psychomotor speed, and visuospatial memory, negatively correlate with the duration of the illness. The most compelling explanation for the observed cognitive decline with longer illness duration in bipolar disorder is likely due to the cumulative effects of repeated mood episodes, chronic stress, and potential neurobiological changes over time. These factors can lead to progressive neurodegeneration and impairments in brain regions critical for cognitive functions, such as the prefrontal cortex and hippocampus.

In our study,the total score of memory among bipolar disorder patients did not significantly differ across varying illness durations. Specifically, at Week 1, the mean total score of memory for groups with illness durations of less than 5 years, 5-10 years, and more than 10 years were 84.62 (SD = 13.30), 86.00 (SD = 12.01), and 85.88 (SD = 10.88), respectively. By Week 3, these scores slightly adjusted to 83.92 (SD = 14.22), 85.33 (SD = 12.87), and 85.80 (SD = 10.94), respectively. At Week 16, the scores further evolved to 81.18 (SD = 14.86), 82.10 (SD = 12.26), and 83.50 (SD = 11.47), respectively, with no significant difference. The change in the total score of memory from Week 1 to Week 3 was minimal: 0.69 (SD = 2.13), 0.67 (SD = 2.67), and 0.08 (SD = 3.25), respectively. The change from Week 1 to Week 16 showed larger variations, being 3.44 (SD = 4.51), 3.90 (SD = 4.12), and 2.38 (SD = 6.39), respectively.

This contrasts with other studies that have reported significant differences in cognitive performance, particularly memory, based on the length of illness duration. Post RM et al. (2007) [165] emphasized that the chronic progression and frequent recurrence of mood episodes in bipolar disorder can significantly impact cognitive functions. They noted that cognitive impairments may vary over time, suggesting that the shorter assessment intervals used in our study may not have been

adequate to effectively capture long-term changes in cognitive performance.

Our study demonstrated that DSST performance was significantly influenced by the duration of illness in bipolar disorder patients. At Week 1, patients with an illness duration of less than 5 years showed a mean DSST score of 36.85 (SD = 14.19), those with 5-10 years of illness registered 35.48 (SD = 11.17), and those with more than 10 years exhibited 24.90 (SD = 10.85), with all groups showing statistically significant differences (p-value < 0.001). This pattern was consistent in Weeks 3 and 16, with notable differences in performance across these illness durations. These observations align with findings from Bhatia P. et al. [11], who also noted a significant correlation between illness duration and cognitive functions like mental speed and set-shifting in bipolar disorder, supported by a Pearson correlation coefficient of 0.326*, indicating a moderate association between illness duration and DSST performance.

Despite these initial differences, the rate of change in DSST performance over time did not show significant variation among the groups across different illness durations. This may be due to the relatively short intervals between assessments in our study (Weeks 1, 3, and 16), which might not be long enough to capture significant long-term changes in cognitive performance, as cognitive shifts can be gradual and may require extended periods to manifest.

Our study revealed that the duration of illness in bipolar disorder significantly affects inflammatory markers, suggesting a link between the chronicity of the condition and an increased inflammatory response. Individuals with a duration of illness greater than 10 years exhibited consistently higher values in these markers at all time points, suggesting a potential exacerbation of inflammatory processes with the progression of the illness. At week 1, we observed significant differences in NLR, MLR, and PLR ($p < 0.001$ for all). By week 3, NLR and PLR continued to show significant differences ($p = 0.004$ for NLR,

$p < 0.001$ for PLR), and by week 16, significant differences persisted in NLR ($p = 0.004$), MLR ($p = 0.002$), and PLR ($p = 0.003$). Although the duration of illness notably influenced these leukocyte ratios at weeks 1, 3, and 16, it did not significantly affect the changes in these ratios over time.

Complementarily, Zeng et al. (2023) [99] reported that NLR may serve as a more relevant biomarker in the chronic stages of the disease, whereas PLR appears to be more indicative in the early stages of bipolar depression. Keshri N. et al. (2018) [80] found that IL-17, a pro-inflammatory cytokine produced by a subset of T cells, correlated positively with the duration of bipolar disorder. There is a noticeable lack of studies that have examined these inflammatory markers over the long term, especially blood count ratios in bipolar disorder. This gap highlights a critical area for future research to understand the chronic impacts of inflammatory responses in Indian populations with bipolar disorder. Further investigation is essential to tailor more effective treatments.

Our study revealed that age was positively correlated with TMT A duration at Weeks 1, 3, and 16, with correlation coefficients of 0.289, 0.366, and 0.382 respectively, indicating that older age was associated with worse performance. However, the change in TMT A durations from baseline to Weeks 3 and 16 were not significantly correlated with age, presenting correlation coefficients of 0.141 and 0.164 respectively. Similarly, TMT B duration at Weeks 1, 3, and 16 showed significant positive correlations with age, with correlation coefficients of 0.386, 0.380, and 0.350, and p-values of less than 0.001 for each. This is consistent with findings by Flaaten et al. (2024) [166], who found that increasing age was linked to poorer psychomotor processing speed. As individuals age, there is a natural decline in cognitive abilities, including slower information processing and reduced efficiency in task-switching and attention. The initial cognitive performance as measured by TMT A and TMT B might reflect the accumulated effects of aging

more clearly, while short-term changes over a few weeks might not show significant variation with age.

The duration of illness was found to be positively correlated with TMT A duration at Weeks 1, 3, and 16 (correlation coefficients: 0.444, 0.451, 0.419; p-values: 0.000, 0.000, 0.000), indicating that longer illness duration was associated with longer TMT A duration. However, the changes in TMT A duration were negatively correlated at Week 3 and significantly at Week 16 (correlation coefficients: -0.183, -0.305; p-values: 0.068, 0.002). TMT B duration showed no significant correlation with illness duration, and the changes in TMT B duration were also not significant. Individuals with longer illness duration may have less cognitive reserve, making it harder for them to improve or maintain cognitive function.

In our study, age negatively correlated with the total score of memory at Weeks 1, 3, and 16, with correlation coefficients of -0.316, -0.303, and -0.245, and corresponding p-values of 0.001, 0.002, and 0.014, respectively, indicating that older age was associated with poorer memory performance. The duration of illness did not significantly correlate with the total score of memory. Studies by Samamé C. et al. [143], Gunning-Dixon FM et al. [167], and Gildengers AG et al. [168, 169] have highlighted medium to large performance deficits, often falling one or more standard deviations below the mean with increasing age. Specific deficits in executive functioning have been identified. Young RC et al. (2006) [170] reported deficits in working memory, verbal memory, attention, and construction among geriatric BD patients, further underscoring the cognitive challenges faced by this population.

DSST scores were found to be negatively correlated with the duration of illness at all assessed weeks (correlation coefficients: -0.426, -0.414, -0.382; p-values < 0.001), suggesting that a longer duration of illness was associated with diminished DSST performance. Conversely, age did not show significant correlations with DSST scores. These results align with prior research, which has demonstrated that prolonged

illness duration can adversely affect cognitive functions, particularly those involving sustained attention and verbal memory, as noted in studies by Van Gorp et al. (1998) [171], Clark et al. (2002) [172], Cavanagh et al. (2002) [173], and Martínez-Arán et al. (2004) [132]. These studies emphasize the impact of illness duration on cognitive performance in tasks that require sustained attention and psychomotor speed, consistent with the broader association between chronic illness and cognitive decline. The absence of a significant correlation with age suggests that factors such as cognitive reserve and the variable effects of aging may help preserve DSST performance despite advancing age.

Age did not showa significant correlation with NLR, MLR, and PLR at Weeks 1, 3, and 16, nor with changes in these markers over time. In contrast, the duration of illness exhibited significant positive correlations with NLR at Week 1 (0.441, $p < 0.001$), Week 3 (0.326, $p = 0.001$), and Week 16 (0.364, $p < 0.001$). MLR also showed significant correlations with the duration of illness at Week 1 (0.314, $p = 0.001$) and Week 3 (0.284, $p = 0.004$), while at Week 16, the correlations were non-significant. PLR demonstrated significant positive correlations in Week 1 (0.492, $p < 0.001$), Week 3 (0.380, $p < 0.001$), and Week 16 (0.333, $p = 0.001$). However, changes in NLR, MLR, and PLR from baseline to Weeks 3 and 16 were generally not significantly correlated with the duration of illness.

The duration of illness markedly influenced immune markers such as NLR, MLR, and PLR, suggesting persistent inflammation in chronic conditions. In contrast, age did not significantly correlate with these markers, which might be due to their stability over shorter time spans or the specific age range included in our study. These observations align with existing literature that links chronic inflammation and immune responses to prolonged illnesses. Supporting this, Van Rheenen et al. (2019) [174] indicated that longer illness durations in bipolar disorder are associated with greater cognitive deficits and elevated inflammatory markers. Furthermore, Kauer-Sant'Anna et al. (2008) [175] found that

TNF-α and IL-6 levels were significantly elevated in early-stage bipolar disorder patients compared to controls, with p-values of 0.002 and <0.001, respectively, and these levels remained high in late-stage patients, with TNF-α levels continuing to be significantly elevated ($p < 0.001$) and IL-6 levels also remaining higher ($p = 0.028$). Additionally, Saglam Aykut D et al. (2017) [47] reported a moderate positive correlation (0.285) between NLR and duration of illness, and a weak positive correlation (0.049) for PLR. These findings collectively underscore the chronic inflammatory response in bipolar disorder and its correlation with illness duration, highlighting the need for further research into anti-inflammatory treatments to manage bipolar disorder.

At Week 1, TMT A duration exhibited significant positive correlations with NLR (rho = 0.211, $p = 0.035$) and PLR (rho = 0.245, $p = 0.014$), suggesting that higher levels of these markers were associated with poorer cognitive performance. This association was further reinforced at Week 3, where TMT A duration significantly correlated with NLR (rho = 0.241, $p = 0.016$), PLR (rho = 0.279, $p = 0.005$), and MLR (rho = 0.215, $p = 0.032$). By Week 16, the significant correlations continued for NLR (rho = 0.270, $p = 0.007$) and PLR (rho = 0.259, $p = 0.009$). Change in TMT A duration from baseline to Week 3 demonstrated strong negative correlations with NLR (rho = -0.345, $p < 0.001$), MLR (rho = -0.238, $p = 0.017$), and PLR (rho = -0.350, $p < 0.001$). Similar patterns were observed from baseline to Week 16, with negative correlations for NLR (rho = -0.479, $p < 0.001$), PLR (rho = -0.359, $p < 0.001$), and MLR (rho = -0.193, $p = 0.055$), indicating that higher levels of inflammation were linked to greater declines in cognitive performance over time.

These findings suggest that baseline levels of inflammation and significant changes over time are more predictive of cognitive performance than minor fluctuations in inflammatory markers. Therefore, managing systemic inflammation could be crucial in addressing cognitive impairments associated with the disorder.

Barbosa IG et al. (2018) [100], Chakrabarty T et al. (2019) [176], and Lotrich FE et al. (2019) [177] observed that individuals with euthymic bipolar disorder patients and poor executive functioning had higher levels of both pro- and anti-inflammatory cytokines compared to controls, with IL-6 showing a negative correlation with overall cognitive performance. Elevated levels of the pro-inflammatory cytokine TNF-α (but not IL-6 or other cytokines) were associated with poorer global cognition, processing speed, and working memory. Additionally, there was an inverse correlation between IL-1RA and processing speed/executive function.

At Weeks 1, 3, and 16, no significant correlations were observed between TMT B duration and the markers NLR, MLR, and PLR. However, increases in PLR were associated with declines in cognitive performance, as a significant negative correlation was found between the change in TMT B duration from baseline to 3 weeks and the change in PLR over the same period. No significant correlations were observed with other markers at Weeks 3 and 16. This indicates that daily or weekly fluctuations in inflammatory markers might be too variable to yield significant correlations unless measured over longer periods or more consistently. Saglam Aykut D et al. (2017) [47] also reported no significant correlation between PLR and neurocognitive tests in their study. Further studies are necessary to investigate the connection between inflammation and cognitive flexibility in bipolar disorder, as current research on this topic is sparse.

In Week 1, there were no significant correlations between the total score of memory and NLR, MLR, or PLR. However, by Week 16, a significant positive correlation was found between NLR at Week 16 and the total score of memory at Week 1 (rho = 0.219, p = 0.029). This suggests that individuals with better initial cognitive performance might have a higher cognitive reserve, providing some protection against the initial effects of inflammation. Over time, persistent or increasing inflammation, as indicated by NLR levels at Week 16, could eventually

become more apparent in relation to earlier cognitive states. At Week 3, no significant correlations were observed between the total score of memory and NLR, MLR, or PLR. By Week 16, the correlations remained non-significant for all markers.

The change in the total score of memory from baseline to 16 weeks showed significant positive correlations with NLR at Week 3 (rho = 0.283, p = 0.004) and NLR at Week 16 (rho = 0.265, p = 0.008). A significant negative correlation was found with the change in NLR from baseline to Week 3 (rho = -0.259, p = 0.009). This suggests that NLR at these specific time points might reflect an acute inflammatory response, potentially beneficial in the short term for cognitive recovery processes, such as synaptic plasticity and neurogenesis. The change in NLR from baseline to Week 16 (rho = -0.297, p = 0.003) also showed significant negative correlations. These findings suggest a complex interaction between inflammatory responses and cognitive performance, particularly with sustained inflammation potentially impacting memory outcomes over time in bipolar disorder patients.

An increase in NLR from baseline to Weeks 3 and 16 may signify a sustained inflammatory burden, negatively impacting brain health and cognitive processes, potentially leading to a decline in memory performance. Doganavsargil-Baysal et al. (2013) [178] also found a negative correlation between inflammatory markers and cognitive function, noting that serum levels of TNF-α and its markers (such as sTNFR1), IL-1, and IL-6 were negatively associated with cognitive function in BD subjects. Elevated levels of pro-inflammatory cytokines in BD patients appeared to be correlated with impaired performance across numerous cognitive domains, including memory, executive function, attention, language, and visuospatial cognition, as reported by Rolstad S (2015) [179] and Barbosa et al. (2012) [180].

In Week 1, PLR demonstrated the strongest negative correlation with DSST scores (ρ = -0.410, p < 0.001), indicating that higher PLR was associated with poorer cognitive performance. NLR and MLR also

showed negative correlations with DSST scores at Week 1, with correlation coefficients of -0.223 ($p = 0.026$) and -0.250 ($p = 0.012$), respectively. By Week 3, these negative correlations persisted, with PLR still showing a strong negative correlation ($\rho = -0.394$, $p < 0.001$) and NLR and MLR continuing to exhibit significant negative correlations with DSST scores. At Week 16, the trend remained, albeit slightly weaker, with PLR ($\rho = -0.342$, $p < 0.001$), NLR ($\rho = -0.217$, $p = 0.030$), and MLR ($\rho = -0.272$, $p = 0.006$) all negatively correlating with DSST scores. Similarly, Rolstad S et al. (2015) [179] reported that patients with bipolar disorder exhibit worse speed/attention scores (Mean = 0.71) compared to controls (Mean = 0.01), alongside higher levels of inflammatory biomarkers such as YKL-40, TIMP1, MCP-1, and sCD14. Additionally, Barbosa et al. (2012) [180] found that global cognitive performance scores on the BAC-A assessment, including symbol coding, correlated negatively with IL-6 levels. The lack of enough data highlights the need for further investigation into the relationship between NLR, MLR, and PLR and cognitive performance in the Indian population.

SUMMARY AND CONCLUSION

Our study involved 100 patients with bipolar disorder and 30 healthy controls, aimed at investigating cognitive functioning andimmune-inflammatory markers, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR) in individuals with bipolar disorder.

1. The majority of cases were aged between 31-40 years (28%), with a mean age of 43 ± 13 years and an average income of Rs. 56,096 ± 65,126.96.

2. Females accounted for 31% of the cases, while males made up the remaining 69%. Among the cases, 82% were married, and 77% belonged to nuclear families. Additionally, 57% of cases lived in urban areas, and 57% followed the Sikh religion. The largest segment within the cases was unemployed individuals, at 45%.

3. There was no notable disparity in age, education, occupation, and marital status between the two groups.

4. A family history of bipolar disorder was noted in 21% of the cases. The majority of the cases, 56%, were on lithium, while 44% were on sodium valproate.

5. In the study, 39% of the cases had an illness duration of less than five years, 21% experienced a duration of five to ten years, and 40% had been ill for more than ten years. The average duration of illness across the cases was ten years, with a standard deviation of 12.6 years.

6. The cases showed notably lower average scores compared to controls in multiple cognitive areas including recent memory, attention and concentration, delayed recall, immediate recall, visual retention, and recognition at weeks 1, 3, and 16.

7. Cases consistently showed significantly lower total scores of memory than controls at weeks 1, 3, and 16. Over 16 weeks, the change in the total score of memory revealed statistically significant differences between cases and controls, with cases exhibiting a more pronounced decline in total score of memory.

8. Cases had significantly lower DSST scores at weeks 1, 3, and 16. The mean change from baseline to 3 weeks between cases and controls had a significant difference, highlighting a decline in processing speed and visual-motor integration skills in the cases.

9. Cases had a significantly higher neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR) compared to controls at weeks 1 and 3, indicating a heightened inflammatory response in the cases.

10. At week 16, cases had significantly higher NLR, MLR, and PLR compared to controls. Cases showed a significant rise in MLR and PLR from baseline to 3 weeks, indicating sustained inflammation and immune system activation.

11. Patients on lithium had significantly higher baseline levels of immune response markers (NLR, MLR, and PLR) at both weeks 3 and 16. However, the sodium valproate group exhibited more significant decline in these markers over time.

12. Sodium valproate and lithium had similar effects on TMT A and TMT B duration over 16 weeks, with no significant differences in cognitive processing speed and cognitive flexibility or their changes over 16 weeks.

13. The sodium valproate group had a total score of memory significantly lower than the lithium group at both weeks 1 and 3. However, over the 16 weeks, the lithium group exhibited a

significantly greater decline in the total score of memory compared to the valproate group.

14. Sodium valproate and lithium had similar effects on DSST performance, showing no significant differences over the 16 weeks.

15. There were no significant gender differences in cognitive processing speed, cognitive flexibility, attention and concentration, working memory, and various other cognitive domains as measured by Trail Making Test A (TMT A) and Trail Making Test B (TMT B) completion times, Digit Symbol Substitution Test (DSST), and total score of memory at weeks 1, 3, and 16, nor in the changes in these scores over the 16 weeks.

16. Females initially exhibited significantly higher inflammatory markers (PLR, NLR, MLR) than males but showed significant reductions in these markers over 16 weeks, indicating a more pronounced decrease in inflammation over time.

17. The duration of illness had no significant impact on the total score of memory at weeks 1, 3, and 16, nor did it impact the changes in the total score of memory at 3 and 16 weeks.

18. The duration of illness significantly affected TMT A duration at weeks 1, 3, and 16, as well as their change (Δ TMT A) from baseline. Longer illness duration was linked with a decline in cognitive processing speed and visual attention tasks (TMT A) over time.

19. The duration of illness significantly affected DSST scores at weeks 1, 3, and 16, with longer illness duration being associated with lower DSST scores, indicating a decline in processing speed and visual-motor coordination.

20. The duration of illness significantly impacted inflammatory markers (NLR, MLR, PLR) at weeks 1, 3, and 16, with longer illness duration being associated with a sustained inflammatory response.

21. Significant positive correlations of age with TMT A and TMT B duration at weeks 1, 3, and 16 indicated that older age was associated with a longer time to complete TMT A and TMT B.

22. Age had a significant negative correlation with the total score of memory at weeks 1, 3, and 16, indicating that memory performance declined with an increase in age in patients with bipolar disorder.

23. The duration of illness revealed significant positive correlations with TMT A duration at weeks 1, 3, and 16 and a significant negative correlation with changes in TMT A over 16 weeks, suggesting that longer illness duration was associated with longer TMT A completion times.

24. The duration of illness revealed significant negative correlations with DSST scores at weeks 1, 3, and 16, indicating that a longer duration of illness was associated with lower DSST scores, reflecting a decline in processing speed, working memory, and attention.

25. The duration of illness exhibited significant positive correlations with inflammatory markers (NLR, MLR, PLR) at weeks 1, 3, and 16, with longer illness duration being associated with a sustained inflammatory response.

26. Higher levels of systemic inflammation were associated with poorer cognitive processing speed and visual attention, as indicated by longer TMT A duration at weeks 1, 3, and 16.

27. Change in TMT A scores (Δ TMT A) from baseline to weeks 3 and 16 had significant negative correlations with the inflammation ratios (NLR, PLR, and MLR).

28. There was a weak negative correlation between change in TMT B over 3 weeks with PLR at Week 3 and a weak positive correlation between change in TMT B over 16 weeks with MLR at Week 16.

29. There was a negative correlation between change in NLR over 3 weeks and 16 weeks and change in the total score of memory over 16 weeks.

30. Higher levels of inflammatory markers (NLR, MLR, PLR) negatively correlated with DSST scores, showing lower cognitive performance at weeks 1, 3, and 16.

CONCLUSION

Our study revealed that individuals with bipolar disorder exhibited lower cognitive performance in several domains, including working memory, attention and concentration, processing speed, cognitive flexibility, visuomotor skills, and executive functions. Additionally, patients with bipolar disorder showed a heightened inflammatory response, evidenced by elevated levels of NLR, MLR, and PLR, which were associated with poorer cognitive outcomes. Specifically, higher levels of these inflammatory markers were significantly linked to lower DSST scores and longer completion times for TMT A and TMT B, highlighting a strong connection between systemic inflammation and deficits in working memory, mental processing speed, and attention. Both the duration of illness and age were found to be significant factors affecting cognitive performance and inflammatory markers, emphasizing the intricate relationship between chronic inflammation and cognitive decline in bipolar disorder. Given the scarcity of research, particularly within the Indian population, further investigation is crucial to better understand these correlations and to develop targeted interventions. The study also noted the impact of mood stabilizers, such as lithium and sodium valproate, on cognitive performance and inflammatory markers, suggesting the importance of considering these effects during treatment planning. This research underscores the necessity for more comprehensive studies to validate these findings and to inform the development of new treatment strategies aimed at reducing cognitive deficits and inflammation in patients with bipolar disorder, ultimately enhancing overall disease management and patient outcomes.

LIMITATIONS

- The study encompassed 100 patients with bipolar disorder and a control group of 30 participants. This relatively small sample size may restrict the generalizability of the results.
- The assessment period spanned 16 weeks with follow-ups at weeks 1, 3, and 16. This duration might not be sufficient to capture long-term cognitive changes and the chronic nature of inflammation in bipolar disorder.
- The study was conducted in a specific geographical region, predominantly involving participants of Sikh and Hindu faiths. This may limit the applicability of the results to other cultural or religious groups.
- The study involved patients treated with either lithium or sodium valproate. Differences in cognitive performance and inflammatory markers between these medications were noted, but the study did not control for other medications that could affect the outcomes.

BIBLIOGRAPHY

1.Chakrabarti S. Bipolar disorder in the International Classification of Diseases-Eleventh version: A review of the changes, their basis, and usefulness. World J Psychiatry. 2022;12:1335-55.

2.Vieta E, Berk M, Schulze TG, Carvalho AF, Suppes T, Calabrese JR, Gao K, Miskowiak KW, Grande I. Bipolar disorders. Nature reviews Disease primers. 2018;4:1-6.

3. Ribeiro J.S., Pereira D., Salagre E., Coroa M., Oliveira P.S., Santos V., Madeira N., Grande I., Vieta E. Risk Calculators in Bipolar Disorder: A Systematic Review.;Brain Sci. 2020;10:525.

4. Krahn G.L. WHO World Report on Disability: A review. [(accessed on 18 September 2020)];Disabil. Health J. 2011 4:141–142

5. Crump C, Sundquist K, Winkleby MA, Sundquist J. Comorbidities and mortality in bipolar disorder: a Swedish national cohort study. JAMA psychiatry. 2013;70:931-9..

6.Nowrouzi B, McIntyre RS, MacQueen G, Kennedy SH, Kennedy JL, Ravindran A, Yatham L, De Luca V. Admixture analysis of age at onset in first episode bipolar disorder. J Affect Disord. 2016;201:88-94

7.Moreno C, Laje G, Blanco C, Jiang H, Schmidt AB, Olfson M. National trends in the outpatient diagnosis and treatment of bipolar disorder in youth. Arch Gen Psychiatry. 2007;64:1032-9.

8.Rowland TA, Marwaha S. Epidemiology and risk factors for bipolar disorder. Ther Adv Psychopharmacol. 2018;8:251-269.

9.Kroon JS, Wohlfarth TD, Dieleman J, Sutterland AL, Storosum JG, Denys D, de Haan L, Sturkenboom MC. Incidence rates and risk factors of bipolar disorder in the general population: a population-based cohort study. Bipolar Disord. 2013;15:306-13.

10.American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.

11. Bhatia P, Sidana A, Das S, Bajaj MK. Neuropsychological functioning in euthymic phase of bipolar affective disorder. Indian J Psychol Med 2018;40:213-8
12. Bearden CE, Hoffman KM, Cannon TD. The neuropsychology and neuroanatomy of bipolar affective disorder: a critical review. Bipolar disorders. 2001;3:106-50.
13. Green MF. What are the functional consequences of neurocognitive deficits in schizophrenia?. The American journal of psychiatry. 1996;153:321-30.
14. Robinson LJ, Nicol Ferrier I. Evolution of cognitive impairment in bipolar disorder: a systematic review of cross-sectional evidence. Bipolar disorders. 2006;8:103-16.
15. Murphy FC, Sahakian BJ. Neuropsychology of bipolar disorder. Br J Psychiatry. 2001;178:S120-7.
16. Doruk A, Ozgen F. Cognitive functions in bipolar disorders. Türkiye KlinikleriDahiliTıpBilimleriDergisiPsikiyatri-TurkiyeKlinikleri J Int Med Sci. 2006;2:23-9.
17. Tuysuzoglu H, Atesci FC, Ozdel O, Oguzoglu NK. Neurological soft signs in bipolar disorder: The impact of comorbid attention deficit hyperactivity disorder neurological soft signs in bipolar disorder: the impact of comorbid attention deficit hyperactivity disorder. NöropsikiyatriArşivi - Archives of Neuropsychiatry 2011;48:107-13.
18. Atagun MI, Balaban OD, Yesilbas D, Keskinkilic C, Evren C. Effect of lateralization on motor and mental speed in bipolar disorder. Klinik PsikofarmakolojiBülteni - Bulletin of Clinical Psychopharmacology 2012;22:297-306.
19. Clark L, Iversen SD, Goodwin GM. A neuropsychological investigation of prefrontal cortex involvement in acute mania. Am J Psychiatry 2001;158:1605-11.
20. Borkowska A and Rybakowski JK. Neuropsychological frontal lobe tests indicate that bipolar depressed patients are more impaired than unipolar. Bipolar Disord2001;3:88- 94.

21.Mur M, Portella MJ, Martı´nez-Ara´n A, Pifarré J, Vieta E. Persistent neuropsychological deficit in euthymic bipolar patients:executive function as a core deficit. J Clin Psychiatry 2007;68:1078-86.
22.Sigurdsson E, Fombonne E, Sayal K, Checkley S. Neurodevelopmental antecedents of early-onset bipolar affective disorder. The British Journal of Psychiatry. 1999;174:121-7.
23.Sole B, BonninCM, Torrent C, Martinez-Aran A, Popovic D, Tabarés-Seisdedos R, et al. Neurocognitive impairment across the bipolar spectrum. CNS Neurosci Ther 2012;18:194-200.
24Ferrier IN, Chowdhury R, Thompson JM, Watson S, Young AH. Neurocognitive function in unaffected first-degree relatives of patients with bipolar disorder: a preliminary report. Bipolar Disord2004;6:319-22.
25.Trivedi JK, Goel D, Dhyani M, Sharma S, Singh AP, Sinha PK, et al. Neurocognition in first-degree healthy relatives (siblings) of bipolar affective disorder patients. Psychiatry Clin Neurosci2008;62:190-6
26.Savitz J, Solms M, Ramesar R. Neuropsychological dysfunction in bipolar affective disorder: a critical opinion. Bipolar Disord2005;7:216-35.
27.Sole B, BonninCM, Torrent C, Martinez-Aran A, Popovic D, Tabarés-Seisdedos R, et al. Neurocognitive impairment across the bipolar spectrum. CNS Neurosci Ther 2012;18:194-200.
28.Grande I, Berk M, Birmaher B, Vieta E. Bipolar disorder. Lancet. 2016;387(10027):1561-1572. doi:10.1016/S0140-6736(15)00241-X.
29.Sigitova E., Fišar Z., Hroudová J., Cikánková T., Raboch J. Biological hypotheses and biomarkers of bipolar disorder. Psychiatry Clin. Neurosci. 2017;71:77–103.
30.Benedetti F., Aggio V., Pratesi M.L., Greco G., Furlan R. Neuroinflammation in bipolar depression. Front. Psychiatry. 2020;11:71.
31.Kowalczyk M., Szemraj J., Bliźniewska K., Maes M., Berk M., Su K.P., Gałecki P. An immune gate of depression—Early neuroimmune development in the formation of the underlying depressive disorder. Pharmacol. Rep. 2019;71:1299–1307.

32. Maes M., Berk M., Goehler L., Song C., Anderson G., Gałecki P., Leonard B. Depression and sickness behavior are janus-faced responses to shared inflammatory pathways. BMC Med. 2012;10:66.
33. Najjar S., Pearlman D.M., Alper K., Najjar A., Devinsky O. Neuroinflammation and psychiatric illness. J. Neuroinflamm. 2013;10:43.
34. Rosenblat J.D. Targeting the immune system in the treatment of bipolar disorder. Psychopharmacology. 2019;236:2909–2921.
35. Fusar-Poli L., Surace T., Vanella A., Meo V., Patania F., Furnari R., et al. The effect of adjunctive nutraceuticals in bipolar disorder: A systematic review of randomized placebo-controlled trials. J. Affect. Disord. 2019;252:334–349.
36. Ashton MM, Kavanagh BE, Marx W, Berk M, Sarris J, Ng CH, et al. A systematic review of nutraceuticals for the treatment of bipolar disorder. The Canadian Journal of Psychiatry. 2021;66:262-73.
37. Misiak B, Bartoli F, Carra G, Małecka M, Samochowiec J, Jarosz K, et al. Chemokine alterations in bipolar disorder: A systematic review and meta-analysis. Brain, Behavior, and Immunity. 2020;88:870-7.
38. Brietzke E., Kauer-Sant'Anna M., Teixeira A.L., Kapczinski F. Abnormalities in serum chemokine levels in euthymic patients with bipolar disorder. BrainBehav. Immun. 2009;23:1079–82.
39. Sayana P, Colpo GD, Simões LR, Giridharan VV, Teixeira AL, Quevedo J, et al. A systematic review of evidence for the role of inflammatory biomarkers in bipolar patients. J Psychiatr Res. 2017;92:160-182.
40. Haarman BC, Riemersma-Van der Lek RF, de Groot JC, Ruhé HG, Klein HC, Zandstra TE, et al. Neuroinflammation in bipolar disorder–A [11C]-(R)-PK11195 positron emission tomography study. Brain behavior, and immunity. 2014;40:219-25.
41. Rao J.S., Harry G.J., Rapoport S.I., Kim H.-W. Increased excitotoxicity and neuroinflammatory markers in postmortem frontal cortex from bipolar disorder patients. Mol. Psychiatry. 2010;15:384–392.

42. Zulfic Z., Weickert C.S., Weickert T.W., Liu D., Myles N., Galletly C.et al.Neutrophil–lymphocyte ratio–a simple, accessible measure of inflammation, morbidity and prognosis in psychiatric disorders? Australas. Psychiatry. 2020;28:454–458
43. Çakır U, Tuman TC, Yıldırım O. Increased neutrophil/lymphoctye ratio in patients with bipolar disorder: a preliminary study. PsychiatrDanub. 2015;27:180-4.
44. Mert D.G., Terzi H. Mean platelet volume in bipolar disorder: The search for an ideal biomarker. Neuropsychiatr. Dis. Treat. 2016;12:2057–2062.
45. Mayda H., Ahsen A., Bağcioğlu E., Öztürk A., Bahçeci B., Soyucok E., et al. Effect of increased neutrophil-to-lymphocyte ratio (NLR) and decreased mean platelet volume (MPV) values on inflammation in acute mania. NöroPsikiyatr. Arşivi. 2016;53:317.
46. Kalelioglu T, Akkus M, Karamustafalioglu N, Genc A, Genc ES, Cansiz A, et al. Neutrophil-lymphocyte and platelet-lymphocyte ratios as inflammation markers for bipolar disorder. Psychiatry Res. 2015;228:925-7.
47. Sağlam Aykut D, Civil Arslan F, ÖzkorumakKaragüzel E, Aral G, Karakullukçu S. The relationship between neutrophil-lymphocyte, platelet–lymphocyte ratio and cognitive functions in bipolar disorder. Nordic Journal of Psychiatry. 2018;72:119-23.
48. Aguglia A., Amerio A., Asaro P., Caprino M., Conigliaro C., Giacomini G., et al. High-lethality of suicide attempts associated with platelet to lymphocyte ratio and mean platelet volume in psychiatric inpatient setting. World J. Biol. Psychiatry. 2020:1–9
49. Ekinci O., Ekinci A. The connections among suicidal behavior, lipid profile and low-grade inflammation in patients with major depressive disorder: A specific relationship with the neutrophil-to-lymphocyte ratio. Nord. J. Psychiatry. 2017;71:574–580.
50. Serafini G., Parisi V.M., Aguglia A., Amerio A., Sampogna G., Fiorillo A., et al. A specific inflammatory profile underlying suicide risk? Systematic review of the main literature findings. Int. J. Environ. Res. Public Health. 2020;17:2393.

51. Mazza MG, Lucchi S, Tringali AG, Rossetti A, Botti ER, Clerici M. et al. Neutrophil/lymphocyte ratio and platelet/lymphocyte ratio in mood disorders: a meta-analysis. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2018;84:229-36.
52. Özdin S, Sarisoy G, Böke Ö. A comparison of the neutrophil-lymphocyte, platelet-lymphocyte and monocyte-lymphocyte ratios in schizophrenia and bipolar disorder patients - a retrospective file review. Nord J Psychiatry. 2017;:509-512.
53. Mazza M.G., Tringali A.G.M., Rossetti A., Botti R.E., Clerici M. Cross-sectional study of neutrophil-lymphocyte, platelet-lymphocyte and monocyte-lymphocyte ratios in mood disorders. Gen. Psychiatry. 2019;58:7–12
54. Rosenblat JD, Brietzke E, Mansur RB, Maruschak NA, Lee Y, McIntyre RS. Et al. Inflammation as a neurobiological substrate of cognitive impairment in bipolar disorder: Evidence, pathophysiology and treatment implications. J Affect Disord. 2015;188:149-59.
55. Inanli I, Aydin M, Çaliskan AM, Eren I. Neutrophil/lymphocyte ratio, monocyte/lymphocyte ratio, and mean platelet volume as systemic inflammatory markers in different states of bipolar disorder. Nordic journal of psychiatry. 2019;73:372-9.
56. Hope S, Melle I, Aukrust P, Steen NE, Birkenaes AB, Lorentzen S, et al. Similar immune profile in bipolar disorder and schizophrenia: selective increase in soluble tumor necrosis factor receptor I and von Willebrand factor. Bipolar disorders. 2009;11:726-34.
57. Huang TL, Lin FC. High-sensitivity C-reactive protein levels in patients with major depressive disorder and bipolar mania. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2007 ;31:370-2.
58. Miller CL, Llenos IC, Dulay JR, Weis S. Upregulation of the initiating step of the kynurenine pathway in postmortem anterior cingulate cortex from individuals with schizophrenia and bipolar disorder. Brain research. 2006;1073:25-37.
59. Köhler O, Sylvia LG, Bowden CL, Calabrese JR, Thase M, Shelton RC, et al. White blood cell count correlates with mood symptom

severity and specific mood symptoms in bipolar disorder. Aust N Z J Psychiatry. 2017;51:355-65.

60Cassidy F, Wilson WH, Carroll BJ. Leukocytosis and hypoalbuminemia in mixed bipolar states: evidence for immune activation. Acta Psychiatrica Scandinavica. 2002;105:60-4.

61.Darko D.F., Rose J., Christian Gillin J., Golshan S., Baird S.M. Neutrophilia and lymphopenia in major mood disorders.1988 25:243–251.

62.Fusar-Poli L, Natale A, Amerio A, Cimpoesu P, Grimaldi Filioli P, Aguglia E, et al. Neutrophil-to-Lymphocyte, Platelet-to-Lymphocyte and Monocyte-to-Lymphocyte Ratio in Bipolar Disorder. Brain Sci. 2021;11:58.

63.Strawbridge R, Carter R, Saldarini F, Tsapekos D, Young AH. Inflammatory biomarkers and cognitive functioning in individuals with euthymic bipolar disorder: exploratory study. BJPsych Open. 2021 Jul;7:e126..

64.Santos JL, Aparicio A, Bagney A, Sánchez-Morla EM, Rodríguez-Jiménez R, Mateo J, et al. A five-year follow-up study of neurocognitive functioning in bipolar disorder. Bipolar Disord. 2014;16:722-31.

65.Pachet AK, Wisniewski AM. The effects of lithium on cognition: an updated review. Psychopharmacology (Berl). 2003;170:225-234.

66.Kim YK, Jung HG, Myint AM, Kim H, Park SH. Imbalance between pro-inflammatory and anti-inflammatory cytokines in bipolar disorder. J Affect Disord. 2007;104:91-5.

67.Sagar R, Sahu A, Pattanayak RD, Chatterjee B. Assessment of cognitive functions in bipolar I disorder: A 1-year naturalistic follow-up study. Bipolar Disord. 2018;20:85-95.

68.Bora E, Yucel M, Pantelis C. Cognitive endophenotypes of bipolar disorder: a meta-analysis of neuropsychological deficits in euthymic patients and their first-degree relatives. J Affect Disord. 2009;113:1-20.

69. Wingo AP, Wingo TS, Harvey PD, Baldessarini RJ. Effects of lithium on cognitive performance: a meta-analysis. J Clin Psychiatry. 2009 ;70:1588-97.
70. Barbosa IG, Rocha NP, Assis F, Vieira ÉL, Soares JC, Bauer ME, et al. Monocyte and lymphocyte activation in bipolar disorder: a new piece in the puzzle of immune dysfunction in mood disorders. International Journal of Neuropsychopharmacology. 2015;18:pyu021.
71. Çakır U, Tuman TC, Yıldırım O. Increased neutrophil/lymphoctye ratio in patients with bipolar disorder: a preliminary study. PsychiatrDanub. 2015;27:180-4.
72. Taj M, Padmavati R. Neuropsychological impairment in bipolar affective disorder. Indian J Psychiatry. 2005;47:48-50.
73. Bauer IE, Keefe RS, Sanches M, Suchting R, Green CE, Soares JC. Evaluation of cognitive function in bipolar disorder using the Brief Assessment of Cognition in Affective Disorders (BAC-A). J Psychiatr Res. 2015;60:81-6.
74. Bora E, Pantelis C. Meta-analysis of cognitive impairment in first-episode bipolar disorder: comparison with first-episode schizophrenia and healthy controls. Schizophrenia bulletin. 2015 ;41:1095-104.
75. Demant KM, Vinberg M, Kessing LV, Miskowiak KW. Assessment of subjective and objective cognitive function in bipolar disorder: Correlations with mood, psychosocial function and the effect of depressive symptoms. J Affect Disord. 2015;170:90-97.
76. Özdin S, Sarisoy G, Böke Ö. A comparison of the neutrophil-lymphocyte, platelet-lymphocyte and monocyte-lymphocyte ratios in schizophrenia and bipolar disorder patients - a retrospective file review. Nord J Psychiatry. 2017;71:509-512.
77. Goyal MK, Solanki RK, Jain A, Yadav KS. Comparison of NLR (neutrophil/lymphocyte ratio) and PLR (platelet/lymphocyte ratio) as inflammatory markers in 1st episode mania and bipolar mania: A preliminary study. Indian J Psychiatry. 2023;65:465-68.

78. Köhler O, Sylvia LG, Bowden CL, Calabrese JR, Thase M, Shelton RC, et al. White blood cell count correlates with mood symptom severity and specific mood symptoms in bipolar disorder. Australian & New Zealand Journal of Psychiatry. 2017;51:355-65.
79. Bora E, Özerdem A. Meta-analysis of longitudinal studies of cognition in bipolar disorder: comparison with healthy controls and schizophrenia. Psychol Med. 2017;47:2753-66.
80. Keshri N, Nandeesha H, Kattimani S. Elevated interleukin-17 and reduced testosterone in Bipolar disorder. Relation with suicidal behaviour. Asian J Psychiatr. 2018;36:37-41.
81. Kirlioglu SS, Balcioglu YH, Kalelioglu T, Erten E, Karamustafalioglu N. Comparison of the complete blood count-derived inflammatory markers in bipolar patients with manic and mixed episodes. Bratisl Lek Listy. 2019;120:195-199
82. Melo MCA, Garcia RF, de Araújo CFC, Abreu RLC, de Bruin PFC, de Bruin VMS. Clinical significance of neutrophil-lymphocyte and platelet-lymphocyte ratios in bipolar patients: An 18-month prospective study. Psychiatry Res. 2019;271:8-14.
83. Lin X, Lu D, Huang Z, Chen W, Luo X, Zhu Y., et al. The associations between subjective and objective cognitive functioning across manic or hypomanic, depressed, and euthymic states in Chinese bipolar patients. J Affect Disord. 2019;249:73-81.
84. Luo X, Zhu Y, Lu D, Zong K, Lin X. Subjective cognitive dysfunction in patients with bipolar disorder: The prevalence, related factors and effects on predicting psychosocial functioning and suicidal ideation. Psychiatry Res. 2020;284:112669.
85. Burdick KE, Millett CE, Russo M, et al. The association between lithium use and neurocognitive performance in patients with bipolar disorder. Neuropsychopharmacology. 2020;45:1743-49.
86. Pigoni A, Mandolini GM, Delvecchio G, Bressi C, Soares JC, Brambilla P, et al. A focus on valproate and cognitive deficits in Bipolar Disorders: A mini-review: Special Section on “Translational and Neuroscience Studies in Affective Disorders” Section Editor,

Maria Nobile MD, PhD. Journal of Affective Disorders. 2020;261:277-81.

87. Fusar-Poli L, Natale A, Amerio A, Cimpoesu P, Grimaldi Filioli P, Aguglia E, et al. Neutrophil-to-Lymphocyte, Platelet-to-Lymphocyte and Monocyte-to-Lymphocyte Ratio in Bipolar Disorder. Brain Sci. 2021;11:58.
88. Xiang R, Xu J, Yu H, Chen Q, Huang Y, Li Z, et al. Effects of carbamazepine and sodium valproate on efficacy, cognitive function and uric acid in epileptic patients with first generalized seizure. Am J Transl Res. 2021;13:9778-83.
89. Bergamelli E, Del Fabro L, Delvecchio G, D'Agostino A, Brambilla P. The Impact of Lithium on Brain Function in Bipolar Disorder: An Updated Review of Functional Magnetic Resonance Imaging Studies. CNS Drugs. 2021;35):1275-87.
90. Cheng Y, Wang Y, Wang X, Jiang Z, Zhu L, Fang S, et al. Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and Monocyte-to-Lymphocyte Ratio in Depression: An Updated Systematic Review and Meta-Analysis. Front Psychiatry. 2022;13:893097.
91. Su M, Ouyang X, Song Y. Neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, and monocyte to lymphocyte ratio in depression: A meta-analysis. J Affect Disord. 2022;308:375-83/
92. Marazziti D, Torrigiani S, Carbone MG, Mucci F, Flamini W, Ivaldi T, Dell'Osso L. Neutrophil/Lymphocyte, Platelet/Lymphocyte, and Monocyte/Lymphocyte Ratios in Mood Disorders. Curr Med Chem. 2022;29:5758-81.
93. Dadouli K, Janho MB, Hatziefthimiou A, et al. Neutrophil-to-Lymphocyte, Monocyte-to-Lymphocyte, Platelet-to-Lymphocyte Ratio and Systemic Immune-Inflammatory Index in Different States of Bipolar Disorder. Brain Sci. 2022;12:1034.
94. Wei Y, Feng J, Ma J, Chen D, Chen J. Neutrophil/lymphocyte, platelet/lymphocyte and monocyte/lymphocyte ratios in patients with affective disorders. J Affect Disord. 2022;309:221-228.

95.Wei Y, Feng J, Ma J, et al. Characteristics of platelet-associated parameters and their predictive values in Chinese patients with affective disorders. BMC Psychiatry. 2022;22:150.
96.Keramatian K, Torres IJ, Yatham LN. Neurocognitive functioning in bipolar disorder: What we know and what we don't. Dialogues Clin Neurosci. 2022;23:29-38.
97 Naseh M, Bayat M, Akbari S, Vatanparast J, Shabani M, Haghighi AB, Haghani M. Neuroprotective effects of sodium valproate on hippocampal cell and volume, and cognitive function in a rat model of focal cerebral ischemia. PhysiolBehav. 2022;251:113806.
98.Hung KC, Liu CC, Wu JY, Ho CN, Lin MC, Hsing CH, et al. Association between the neutrophil-to-lymphocyte ratio and cognitive impairment: a meta-analysis of observational studies. Front Endocrinol (Lausanne). 2023;14:1265637.
99.Zeng J, Zhang Y, Xiang Y, et al. Optimizing multi-domain hematologic biomarkers and clinical features for the differential diagnosis of unipolar depression and bipolar depression. npj Mental Health Res 2023;2:4.
100Barbosa IG, de Almeida Ferreira R, Rocha NP, Mol GC, Leite FD, Bauer IE, et al. Predictors of cognitive performance in bipolar disorder: the role of educational degree and inflammatory markers. Journal of psychiatric research. 2018;106:31-7.
101.Chen MH, Hsu JW, Huang KL, Tsai SJ, Su TP, Li CT, et al. Role of obesity in systemic low-grade inflammation and cognitive function in patients with bipolar I disorder or major depressive disorder. CNS Spectr. 2021;26:521-27.
102.Poletti S, Mazza MG, Calesella F, Vai B, Lorenzi C, Manfredi E, et al. Circulating inflammatory markers impact cognitive functions in bipolar depression. J Psychiatr Res. 2021;140:110-116.
103.Sæther LS, Ueland T, Haatveit B, Maglanoc LA, Szabo A, Djurovic S, et al. Inflammation and cognition in severe mental illness: patterns of covariation and subgroups. Mol Psychiatry. 2023;28:1284-92.
104.Pattanayak RD, Sagar R, Mehta M. Neuropsychological performance in euthymic Indian patients with bipolar disorder type I: Correlation

between quality of life and global functioning. Psychiatry Clin Neurosci 2012; 66:553-63.

105. Nehra R, Chakrabarti S, Pradhan BK, Khehra N. Comparison of cognitive functions between first- and multi-episode bipolar affective disorders. J Affect Disord 2006;93:185-92.

106. Pradhan BK, Chakrabarti S, Nehra R, Mankotia A. Cognitive functions in bipolar affective disorder and schizophrenia: Comparison. Psychiatry Clin Neurosci 2008;62:515-25.

107. Trivedi JK, Dhyani M, Sharma S, Sinha PK, Singh AP, Tandon R. Cognitive functions in euthymic state of bipolar disorder: An Indian study. Cogn Neuropsychiatry 2008;13:135-47.

108 Goswami U, Sharma A, Varma A, Gulrajani C, Ferrier IN, Young AH, et al. The neurocognitive performance of drugfree and medicated euthymic bipolar patients do not differ. Acta Psychiatr Scand 2009; 120:456-63.

109 Kulkarni S, Jain S, Janardhan Reddy YC, Kumar KJ, Kandavel T. Impairment of verbal learning and memory and executive function in unaffected siblings of probands with bipolar disorder. Bipolar Disord 2010;12:647-56.

110 Pattanayak RD, Sagar R, Mehta M. Cognitive dysfunction as a trait marker for bipolar disorder: a critical review. J Ment Health Hum Behav. 2011;16:18-28.

111 Goyal MK, Solanki RK, Jain A, Yadav KS. Comparison of NLR (neutrophil/lymphocyte ratio) and PLR (platelet/lymphocyte ratio) as inflammatory markers in 1st episode mania and bipolar mania: A preliminary study. Indian Journal of Psychiatry. 2023;65:465-8.

112 Dhiman S, Subodh BN, Chakrabarti S. Course and outcome of bipolar I disorder among Indian patients: A retrospective life-chart study. Indian J Psychiatry. 2022;64:510-17.

113 Grover S, Avasthi A, Chakravarty R, Dan A, Chakraborty K, Neogi R, Desouza A, et al. Subjective cognitive deficits and its correlates among patients with bipolar disorder: Findings from the bipolar disorder course and outcome study from India (BiD-CoIN study). Indian Journal of Psychiatry. 2023;65:345-55.

114 Grant BF, Goldstein RB, Chou SP, Huang B, Stinson FS, Dawson DA, et al. Sociodemographic and psychopathologic predictors of first incidence of DSM-IV substance use, mood and anxiety disorders: results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. Molecular psychiatry. 2009;14:1051-66.

115 Verma KK, Garg SK, Baniya GC, Singh H. Neuro-cognition in patients of bipolar affective disorder (currently in remission) and their first degree healthy relatives. Int J Med Sci Public Health 2016;5:2429-34

116 Reddy MS, Rao GP, Kumar S, Seshadri V, Prasant P. Clinical characteristics, sociodemographic profile, and treatment pattern of bipolar disorder - A multicenter study from India. Psycom. 2022;100039.

117 Craddock, N., & Jones, I. (1999). "Genetics of bipolar disorder." Journal of Medical Genetics 36.8: 585-594.

118. El Safy ER, El Masry NM, El Shabrawy A, Ellatif AR. Neurological soft signs for discrimination between euthymic patients with bipolar I disorder and healthy controls. Middle East Current Psychiatry. 2020 ;27:1-7.

119. Gershon ES, Hamovit J, Guroff JJ, Dibble E, Leckman JF, Sceeryet al. A family study of schizoaffective, bipolar I, bipolar II, unipolar, and normal control probands. Archives of General psychiatry. 1982;39:1157-67.

120. Grover S, Hazari N, Aneja J, Chakrabarti S, Avasthi A. Influence of religion and supernatural beliefs on clinical manifestation and treatment practices in patients with bipolar disorder. Nordic Journal of Psychiatry. 2016;70:442-9.

121. Reddy MS, Rao GP, Kumar S, Seshadri V, Prasant P. Clinical characteristics, sociodemographic profile, and treatment pattern of bipolar disorder - A multicenter study from India. J Psychiatr Res. 2021;56:42-49.

122. Swaroopachary RS, Kalasapati LK, Ivaturi SC, Reddy CMPK. Disability in bipolar affective disorder patients in relation to the

duration of illness and current affective state. Arch Ment Health. 2018;19:37.

123 Ancin I, Cabranes JA, Santos JL, Sanchez-Morla E, Vazquez-Alvarez B, et al. CHRNA7 haplotypes are associated with impaired attention in euthymic bipolar disorder. Journal of affective disorders. 2011;133:340-5.

124. Brooks JR, Bearden CE, Hoblyn JC, Woodard SA, Ketter TA. Prefrontal and paralimbic metabolic dysregulation related to sustained attention in euthymic older adults with bipolar disorder. Bipolar Disord. 2010;12:866–74.

125. Calabrò M, Mandelli L, Crisafulli C, Sidoti A, Jun TY, Lee SJ, Han C, et al. Genes involved in neurodevelopment, neuroplasticity, and bipolar disorder: CACNA1C, CHRNA1, and MAPK1. Neuropsychobiology. 2017;74:159-68.

126 Newton DF, Naiberg MR, Andreazza AC, Scola G, Dickstein DP, Goldstein BI, et al. Association of lipid peroxidation and brain-derived neurotrophic factor with executive function in adolescent bipolar disorder. Psychopharmacology. 2017;234:647-56.

127. Mora E, Portella MJ, Piñol-Ripoll G, López R, Cuadras D, Forcada I, et al. High BDNF serum levels are associated to good cognitive functioning in bipolar disorder. European Psychiatry. 2019;60:97-107.

128. Ni P, Ma X, Lin Y, Lao G, Hao X, Guan Let al. Methionine sulfoxide reductase A (MsrA) associated with bipolar I disorder and executive functions in A Han Chinese population. Journal of affective disorders. 2015;184:235-8.

129. Vasconcelos-Moreno MP, Fries GR, Gubert C, Dos Santos BT, Fijtman A, Sartori J, et al. Telomere length, oxidative stress, inflammation and BDNF levels in siblings of patients with bipolar disorder: implications for accelerated cellular aging. International Journal of Neuropsychopharmacology. 2017;20:445-54.

130 Dittmann S, Seemüller F, Schwarz MJ, Kleindienst N, Stampfer R, Zach J, et al. Association of cognitive deficits with elevated homocysteine levels in euthymic bipolar patients and its impact on

psychosocial functioning: preliminary results. Bipolar Disorders. 2007;9:63-70.

131. Calkin CV. Insulin resistance takes center stage: a new paradigm in the progression of bipolar disorder. Ann Med. 2019;51:281–93.

132 Martínez-Arán A, Vieta E, Reinares M, Colom F, Torrent C, Sánchez-Moreno J, et al. Cognitive function across manic or hypomanic, depressed, and euthymic states in bipolar disorder. American Journal of Psychiatry. 2004;161:262-70.

133. Arts B, Jabben N, Krabbendam L, van Os J. Meta-analyses of cognitive functioning in euthymic bipolar patients and their first-degree relatives. Psychol Med. 2008;38:771-85.

134. Torres IJ, Boudreau VG, Yatham LN. Neuropsychological functioning in euthymic bipolar disorder: a meta-analysis. Acta Psychiatr Scand Suppl. 2011;123:17-26.

135. Ekman CJ, Lind J, Ryden E, et al. Neurocognitive function in bipolar disorder: a comparison between bipolar I and II disorder and matched controls. BMC Psychiatry. 2020;20:261.

136. Bora E, Özerdem A. Neuropsychological functioning in bipolar depression: a meta-analysis of comparative studies. J Affect Disord. 2017;210:258-68.

137. Torrent C, Bonnin CM, Martinez-Aran A, et al. Long-term outcome of cognitive impairment in bipolar disorder. J Clin Psychiatry. 2012;73.

138. MacQueen GM, Memedovich KA. Cognitive dysfunction in major depression and bipolar disorder: assessment and treatment options. Psychiatry Clin Neurosci. 2017;71:18-27.

139. Krabbendam L, Arts B, van Os J, Aleman A. Cognitive functioning in patients with schizophrenia and bipolar disorder: a quantitative review. Schizophr Res. 2005;80:137–149.

140. Lewandowski KE, Sperry SH, Malloy MC, Forester BP. A cross-sectional study of cognitive performance in bipolar disorder across the lifespan: the cog-BD project. Psychol Med. 2014;44:987-1000.

141. Ganesh UM, Shwetha TS, Bhandary RP. Social Cognition and Neuro-cognition in Patients with Bipolar Disorder, Their First-Degree Relatives and Healthy Controls. J Psychiatric Res. 2021;55:45-53.

142 López-Jaramillo C, Lopera-Vásquez J, Gallo A, Ospina-Duque J, Bell V, Torrent C, Martínez-Arán A, et al. Effects of recurrence on the cognitive performance of patients with bipolar I disorder: implications for relapse prevention and treatment adherence. Bipolar disorders. 2010;12:557-67.

143. Samamé C, Martino DJ, Strejilevich SA. A cross-sectional study of cognitive performance in bipolar disorder across the lifespan: the cog-BD project. Psychol Med. 2014;44:2049-58.

144. Barbosa IG, Bauer ME, MacHado-Vieira R, Teixeira AL. Cytokines in bipolar disorder: Paving the way for neuroprogression. Rev Bras Psiquiatr. 2014;36:129-36.

145. McNamara RK, Lotrich FE. Elevated immune-inflammatory signaling in mood disorders: a new therapeutic target? Expert Rev Neurother. 2012;12:1143-61.

146 Rosenblat JD, McIntyre RS. Bipolar disorder and inflammation. Psychiatric Clinics. 2016;39:125-37.

147. Mayda H, Ahsen A, Bağcıoğlu E, Öztürk A, Bahçeci B, Soyuçok E, et al. Effect of Increased Neutrophil-to-Lymphocyte Ratio (NLR) and Decreased Mean Platelet Volume (MPV) Values on Inflammation in Acute Mania. GynecolObstet Invest. 2024;89:140-49.

148 Kalelioglu T, Akkus M, Karamustafalioglu N, Genc A, Genc ES, Cansiz A, Emul M. Neutrophil-lymphocyte and platelet-lymphocyte ratios as inflammation markers for bipolar disorder. Psychiatry Res. 2015;228(3):925-927.

149 La Verde M, Luciano M, Fordellone M, et al. Postpartum Depression and Inflammatory Biomarkers of Neutrophil-Lymphocyte Ratio, Platelet-Lymphocyte Ratio, and Monocyte-Lymphocyte Ratio: A Prospective Study. GynecolObstet Invest. 2024;89:140-149.

150. Ozdin S, Ozdin SB. A comparison of the neutrophil-lymphocyte, platelet-lymphocyte and monocyte-lymphocyte ratios in schizophrenia and bipolar disorder patients - a retrospective file review. Nord J Psychiatry. 2020;74:444-450

151.Berk M, Kapczinski F, Andreazza AC, Dean OM, Giorlando F, Maes M, et al. Pathways underlying neuroprogression in bipolar disorder: focus on inflammation, oxidative stress and neurotrophic factors. NeurosciBiobehav Rev. 2011;35:804-17.

152Balanzá-Martínez V, Rubio C, Selva-Vera G, Martinez-Aran A, Sanchez-Moreno J, Salazar-Fraile J, et al. Neurocognitive endophenotypes (endophenocognitypes) from studies of relatives of bipolar disorder subjects: a systematic review. Neuroscience & Biobehavioral Reviews. 2008;32:1426-38.

153.Lund Y, Nissen M, Rafaelsen OJ. Long-term lithium treatment and psychological functions. Acta Psychiatrica Scandinavica. 1982 ;65:233-44.

154 Wingo AP, Wingo TS, Harvey PD, Baldessarini RJ. Effects of lithium on cognitive performance: a meta-analysis. J Clin Psychiatry. 2009;70:1588-97.

155.Gould TD, Manji HK. The Wnt signaling pathway in bipolar disorder. The Neuroscientist. 2002;8:497-511.

156.Jope RS. Lithium and GSK-3: one inhibitor, two inhibitory actions, multiple outcomes. Trends Pharmacol Sci. 2003;24:441-43.

157. Beurel E, Jope RS. The paradoxical pro-and anti-apoptotic actions of GSK3 in the intrinsic and extrinsic apoptosis signaling pathways. Progress in neurobiology. 2006;79:173-89..

158.Mur M, Portella MJ, Martínez-Arán A, Pifarré J, Vieta E. Long-term stability of cognitive impairment in bipolar disorder: a 2-year follow-up study of lithium-treated euthymic bipolar patients. J Clin Psychiatry. 2008;69:712-19.

159.Muralidharan K, Kozicky JM, Bücker J, Silveira LE, Torres IJ, Yatham LN, et al Are cognitive deficits similar in remitted early bipolar I disorder patients treated with lithium or valproate? Data from the STOP-EM study. European Neuropsychopharmacology. 2015 ;25:223-30.

160.Tombaugh TN. Trail Making Test A and B: normative data stratified by age and education. Archives of clinical neuropsychology. 2004 ;19:203-14.

161.Lee J, Shih R, Feeney K, Langa KM. Gender disparity in late-life cognitive functioning in India: findings from the longitudinal aging study in India. J Gerontol B Psychol Sci Soc Sci. 2014;69:603-11.

162.Langa KM, Larson EB, Karlawish JH, Cutler DM, Kabeto MU, Kim SY, et al. Trends in the prevalence and mortality of cognitive impairment in the United States: is there evidence of a compression of cognitive morbidity?. Alzheimer's & Dementia. 20081;4:134-44.

163.Royall DR, Palmer R, Chiodo LK, Polk MJ. Declining executive control in normal aging predicts change in functional status: the Freedom House Study. Journal of the American Geriatrics Society. 2004;52:346-52.

164.Lee JS, Kim NY, Na SH, Youn YH, Shin CS. Reference values of neutrophil-lymphocyte ratio, lymphocyte-monocyte ratio, platelet-lymphocyte ratio, and mean platelet volume in healthy adults in South Korea. Medicine (Baltimore). 2018;97.

165 Post RM. Mechanisms of illness progression in the recurrent affective disorders. Neurotox Res. 2007;12:3-18.

166.Flaaten CB, Melle I, Bjella T, Engen MJ, Åsbø G, Wold KF, et al. Long-term course of cognitive functioning in bipolar disorder: A ten-year follow-up study. Bipolar Disord. 2024;26:136-147.

167.Gunning-Dixon FM, Murphy CF, Alexopoulos GS, Majcher-Tascio M, Young RC. Executive dysfunction in elderly bipolar manic patients. The American journal of geriatric psychiatry. 2008;16:506-12.

168.Gildengers AG, Butters MA, Seligman K, McShea M, Miller MD, Mulsant BH, et al. Cognitive functioning in late-life bipolar disorder. American Journal of Psychiatry. 2004;161:736-8.

169.Gildengers AG, Mulsant BH, Al Jurdi RK, Beyer JL, Greenberg RL, Gyulai L, et al. The relationship of bipolar disorder lifetime duration and vascular burden to cognition in older adults. Bipolar disorders. 2010;12:851-8.

170 Young RC, Murphy CF, Heo M, Schulberg HC, Alexopoulos GS. Cognitive impairment in bipolar disorder in old age: literature review and findings in manic patients. Journal of Affective Disorders. 2006 ;92:125-31.

171. Van Gorp WG, Altshuler L, Theberge DC, Wilkins J, Dixon W. Cognitive impairment in euthymic bipolar patients with and without prior alcohol dependence. Arch Gen Psychiatry. 1998;55:41-46.
172. Clark L, Iversen SD, Goodwin GM. Sustained attention deficit in bipolar disorder. Br J Psychiatry. 2002;180:313-319.
173. Cavanagh JTO, Van Beck M, Muir W, Blackwood DH. Case-control study of neurocognitive function in euthymic patients with bipolar disorder: an association with mania. Br J Psychiatry. 2002;180:320-326.
174. Van Rheenen TE, Lewandowski KE, Bauer IE, Kapczinski F, Miskowiak K, Burdick KE, et al. Current understandings of the trajectory and emerging correlates of cognitive impairment in bipolar disorder: An overview of evidence. Bipolar Disord. 2020;22:13-27.
175 Kauer-Sant'Anna M, Kapczinski F, Andreazza AC, Bond DJ, Lam RW, Young LT, et al. Brain-derived neurotrophic factor and inflammatory markers in patients with early-vs. late-stage bipolar disorder. International Journal of Neuropsychopharmacology. 2009 ;12:447-58.
176 Chakrabarty T, Torres IJ, Bond DJ, Yatham LN. Inflammatory cytokines and cognitive functioning in early-stage bipolar I disorder. J Affect Disord 2019;245:679–85.
177. Lotrich FE, Butters MA, Aizenstein H, Marron MM, Reynolds CF III, Gildengers AG, et al The relationship between interleukin-1 receptor antagonist and cognitive function in older adults with bipolar disorder. Int J Geriatr Psychiatry. 2014;29:1246-54..
178. Doganavsargil-Baysal O, Cinemre B, Aksoy UM, Akbas H, Metin O, Fettahoglu C, et al. Levels of TNF-α, soluble TNF receptors (sTNFR1, sTNFR2), and cognition in bipolar disorder. Human Psychopharmacology: Clinical and Experimental. 2013;28:160-7..
179. Rolstad S, Jakobsson J, Sellgren C, Isgren A, Ekman CJ, Bjerke M, et al. CSF neuroinflammatory biomarkers in bipolar disorder are associated with cognitive impairment. European neuropsychopharmacology. 2015 ;25:1091-8..
180. Barbosa IG, Rocha NP, Huguet RB, Ferreira RA, Salgado JV, Carvalho LA, Pariante CM, Teixeira AL, et al Executive dysfunction

in euthymic bipolar disorder patients and its association with plasma biomarkers. J Affect Disord. 2012;136.

SR. NO	NAME	MRD . NO	GROUP	AGE	SEX	MARITAL STATUS	EDUCATION	OCCUPATION	FAMILY TYPE	RELIGION	RESIDENCE	INCOME	DURATION OF ILLNESS (YEARS)	FAMILY HISTORY OF PSYCHIATRIC ILLNESS	MOOD STABILIZERS
1	RS	45720	CASES	59	MALE	MARRIED	MATRICULATION	UNEMPLOYED	NUCLEAR	SIKH	RURAL	30000	27	ABSENT	SODIUM VALPROATE
2	S	135050	CASES	28	MALE	UNMARRIED	GRADUATION	PROFESSIONAL	NUCLEAR	HINDU	URBAN	28000	9	ABSENT	LITHIUM
3	RK	99886	CASES	40	FEMALE	MARRIED	POST-GRADUATE	UNEMPLOYED	NUCLEAR	SIKH	URBAN	18900	40	ABSENT	LITHIUM
4	JK	850319	CASES	52	MALE	MARRIED	PRIMARY	SEMISKILLED	NUCLEAR	SIKH	RURAL	7000	1	ABSENT	SODIUM VALPROATE
5	AD	1158930	CASES	40	FEMALE	MARRIED	PRIMARY	UNEMPLOYED	JOINT	HINDU	RURAL	77000	35	ABSENT	LITHIUM
6	RS	1759698	CASES	64	MALE	MARRIED	MATRICULATION	SEMIPROFESSIONAL	NUCLEAR	HINDU	RURAL	20000	11	ABSENT	LITHIUM
7	VK	62916	CASES	31	FEMALE	MARRIED	POST-GRADUATE	PROFESSIONAL	NUCLEAR	SIKH	RURAL	15000	7	PRESENT	LITHIUM
8	PK	1443712	CASES	21	FEMALE	UNMARRIED	GRADUATION	UNEMPLOYED	NUCLEAR	SIKH	RURAL	160000	1	ABSENT	LITHIUM
9	RK	1634315	CASES	38	FEMALE	MARRIED	POST-GRADUATE	UNEMPLOYED	NUCLEAR	SIKH	URBAN	50,000	5	ABSENT	LITHIUM
10	KS	1642409	CASES	52	MALE	MARRIED	PRIMARY	UNSKILLED	JOINT	SIKH	RURAL	89000	2	ABSENT	LITHIUM
11	M	1199536	CASES	40	FEMALE	MARRIED	MATRICULATION	UNEMPLOYED	NUCLEAR	HINDU	URBAN	10000	5	ABSENT	LITHIUM
12	GS	1541709	CASES	36	MALE	MARRIED	HIGHER SECONDARY	SEMISKILLED	JOINT	SIKH	RURAL	40,000	3	ABSENT	SODIUM VALPROATE
13	SB	37941	CASES	57	FEMALE	MARRIED	MATRICULATION	UNEMPLOYED	NUCLEAR	HINDU	URBAN	300000	8	ABSENT	SODIUM VALPROATE
14	VL	38770	CASES	46	FEMALE	MARRIED	PRIMARY	UNEMPLOYED	JOINT	HINDU	URBAN	30000	2	ABSENT	SODIUM VALPROATE
15	JS	74019	CASES	46	MALE	MARRIED	MATRICULATION	SEMISKILLED	NUCLEAR	SIKH	RURAL	15,000	6	ABSENT	SODIUM VALPROATE
16	S	1049140	CASES	26	MALE	UNMARRIED	MIDDLE SCHOL	SKILLED WORKER	JOINT	SIKH	RURAL	8000	32	ABSENT	LITHIUM
17	IS	1339870	CASES	49	MALE	MARRIED	MIDDLE SCHOL	SKILLED WORKER	NUCLEAR	SIKH	RURAL	20,000	10	ABSENT	SODIUM VALPROATE
18	JK	1132829	CASES	23	MALE	UNMARRIED	GRADUATION	UNEMPLOYED	NUCLEAR	HINDU	URBAN	20000	3	ABSENT	LITHIUM
19	GS	199826	CASES	55	MALE	MARRIED	MATRICULATION	SKILLED WORKER	NUCLEAR	SIKH	RURAL	70000	20	ABSENT	LITHIUM
20	GK	1565812	CASES	32	FEMALE	UNMARRIED	GRADUATION	UNEMPLOYED	NUCLEAR	SIKH	URBAN	80000	12	PRESENT	LITHIUM
21	MS	1151573	CASES	32	MALE	MARRIED	GRADUATION	SEMISKILLED	NUCLEAR	SIKH	URBAN	60,000	1	ABSENT	SODIUM VALPROATE
22	SK	91953	CASES	57	FEMALE	MARRIED	GRADUATION	UNEMPLOYED	NUCLEAR	SIKH	URBAN	50,000	5	ABSENT	SODIUM VALPROATE
23	KK	1538796	CASES	47	FEMALE	MARRIED	PRIMARY	UNEMPLOYED	NUCLEAR	SIKH	RURAL	19000	22	ABSENT	SODIUM VALPROATE
24	RS	74094	CASES	52	MALE	MARRIED	MATRICULATION	SEMISKILLED	JOINT	SIKH	RURAL	10,000	22	ABSENT	SODIUM VALPROATE
25	PG	1528192	CASES	39	FEMALE	MARRIED	GRADUATION	UNEMPLOYED	NUCLEAR	HINDU	URBAN	60000	12	ABSENT	LITHIUM
26	AK	59642	CASES	63	MALE	MARRIED	GRADUATION	UNEMPLOYED	NUCLEAR	HINDU	URBAN	88000	20	ABSENT	LITHIUM
27	HK	1762751	CASES	43	FEMALE	MARRIED	HIGHER SECONDARY	UNEMPLOYED	NUCLEAR	SIKH	RURAL	80000	3	ABSENT	LITHIUM
28	KS	71428	CASES	56	MALE	MARRIED	MIDDLE SCHOL	UNSKILLED	NUCLEAR	SIKH	RURAL	6000	2	PRESENT	SODIUM VALPROATE
29	MH	52615	CASES	61	MALE	MARRIED	GRADUATION	SEMISKILLED	NUCLEAR	HINDU	URBAN	40,000	40	ABSENT	SODIUM VALPROATE
30	UR	1202853	CASES	48	FEMALE	MARRIED	GRADUATION	UNEMPLOYED	NUCLEAR	HINDU	RURAL	18000	15	PRESENT	LITHIUM
31	GS	831727	CASES	55	MALE	MARRIED	MATRICULATION	SEMISKILLED	NUCLEAR	SIKH	RURAL	200000	2	PRESENT	SODIUM VALPROATE
32	CS	1442784	CASES	48	MALE	MARRIED	MATRICULATION	SEMISKILLED	NUCLEAR	SIKH	RURAL	100000	33	PRESENT	LITHIUM
33	LD	37575	CASES	48	FEMALE	MARRIED	MATRICULATION	UNEMPLOYED	NUCLEAR	HINDU	URBAN	20000	8	ABSENT	LITHIUM
34	S	1488612	CASES	56	FEMALE	MARRIED	POST-GRADUATE	UNEMPLOYED	NUCLEAR	HINDU	URBAN	50000	2	ABSENT	LITHIUM
35	BK	1534840	CASES	42	MALE	MARRIED	GRADUATION	UNEMPLOYED	JOINT	HINDU	URBAN	40000	2	ABSENT	SODIUM VALPROATE
36	BR	115718	CASES	68	MALE	MARRIED	MATRICULATION	UNEMPLOYED	NUCLEAR	HINDU	URBAN	30000	33	ABSENT	SODIUM VALPROATE
37	GS	1695223	CASES	55	MALE	MARRIED	MIDDLE SCHOL	SEMISKILLED	NUCLEAR	SIKH	RURAL	10000	10	PRESENT	LITHIUM
38	PS	93624	CASES	27	MALE	MARRIED	MATRICULATION	SEMISKILLED	NUCLEAR	SIKH	RURAL	40000	3	ABSENT	SODIUM VALPROATE
39	RG	1195183	CASES	50	MALE	MARRIED	MATRICULATION	SEMIPROFESSIONAL	JOINT	HINDU	URBAN	65000	26	ABSENT	LITHIUM
40	GS	1529782	CASES	34	MALE	MARRIED	HIGHER SECONDARY	SEMISKILLED	JOINT	SIKH	URBAN	50000	3	ABSENT	LITHIUM
41	BS	1539625	CASES	65	MALE	MARRIED	MATRICULATION	PROFESSIONAL	JOINT	SIKH	URBAN	29000	5	ABSENT	LITHIUM
42	GS	352125	CASES	60	MALE	MARRIED	GRADUATION	UNEMPLOYED	NUCLEAR	SIKH	URBAN	50000	10	ABSENT	SODIUM VALPROATE
43	SR	79111	CASES	43	FEMALE	MARRIED	POST-GRADUATE	PROFESSIONAL	NUCLEAR	HINDU	URBAN	10000	30	ABSENT	LITHIUM
44	PS	1539699	CASES	20	MALE	UNMARRIED	DIPLOMA	UNEMPLOYED	NUCLEAR	SIKH	URBAN	15000	1	ABSENT	SODIUM VALPROATE
45	BS	1653458	CASES	34	MALE	MARRIED	GRADUATION	UNEMPLOYED	NUCLEAR	SIKH	RURAL	40000	15	ABSENT	SODIUM VALPROATE
46	SS	296473	CASES	44	MALE	MARRIED	MATRICULATION	SEMISKILLED	NUCLEAR	SIKH	URBAN	40000	6	ABSENT	SODIUM VALPROATE
47	DS	156621	CASES	46	MALE	MARRIED	MATRICULATION	SEMISKILLED	JOINT	SIKH	RURAL	20000	10	ABSENT	SODIUM VALPROATE
48	J	1745061	CASES	29	MALE	UNMARRIED	GRADUATION	UNEMPLOYED	NUCLEAR	SIKH	RURAL	10000	3	PRESENT	LITHIUM
49	JS	1762466	CASES	63	MALE	MARRIED	MATRICULATION	SEMISKILLED	JOINT	HINDU	RURAL	70000	10	ABSENT	LITHIUM
50	M	1421879	CASES	25	MALE	UNMARRIED	GRADUATION	SEMIPROFESSIONAL	JOINT	HINDU	URBAN	200000	2	ABSENT	SODIUM VALPROATE

SR. NO	NAME	MRD . NO	TMTA week 1	TMTA week 3	TMTA week 16	Δ TMTA week 3	Δ TMTA week 16	TMTB week 1	TMTB week 3	TMTB week 16	Δ TMTB week 3	Δ TMTB week 16	DIGIT FORWARD WEEK 1	DIGIT FORWARD WEEK 3	DIGIT FORWARD WEEK 16	DIGIT BACKWARD WEEK 1	DIGIT BACKWARD WEEK 3	DIGIT BACKWARD WEEK 16	REMOTE MEMORY WEEK 1
1	RS	45720	111	90	98	21	13	100	86	79	14	21	5	5	5	4	4	4	5
2	S	135050	29	24	20	5	9	82	68	61	14	21	5	6	5	3	2	2	6
3	RK	99886	58	55	45	3	13	105	90	84	15	21	6	7	6	5	5	4	6
4	JK	850319	70	60	57	10	13	120	108	95	12	25	5	4	4	4	4	4	6
5	AD	1158930	190	250	280	-60	-90	240	226	201	14	39	3	3	2	2	2	2	6
6	RS	1759698	93	83	80	10	13	178	170	146	8	32	5	5	5	4	4	4	6
7	VK	62916	36	38	23	-2	13	74	76	77	-2	-3	7	6	6	3	2	2	6
8	PK	1443712	43	40	30	3	13	127	98	67	29	60	7	7	6	5	5	4	6
9	RK	1634315	35	40	22	-5	13	58	60	95	-2	-37	7	7	6	4	4	4	6
10	KS	1642409	52	50	39	2	13	128	117	100	11	28	6	5	5	4	3	3	6
11	M	1199536	100	110	87	-10	13	240	250	200	-10	40	4	4	5	2	2	2	6
12	GS	1541709	100	36	87	64	13	90	88	83	2	7	4	3	3	4	2	2	6
13	SB	37941	312	278	299	34	13	459	403	371	56	88	5	5	4	3	2	2	5
14	VL	38770	58	60	90	-2	-32	89	80	72	9	17	5	5	5	5	5	4	5
15	JS	74019	66	60	53	6	13	123	130	164	-7	-41	4	4	4	2	2	2	6
16	S	1049140	160	250	387	-90	-227	180	150	100	30	80	6	4	4	4	3	3	6
17	IS	1339870	36.2	32	23.2	4.2	13	63	57	50	6	13	3	4	3	3	2	2	5
18	JK	1132829	25	24	12	1	13	76	60	61	16	15	8	7	6	5	5	4	6
19	GS	199826	70	65	57	5	13	129	115	108	14	21	4	4	4	4	4	4	6
20	GK	1565812	44	40	31	4	13	218	100	197	118	21	5	4	4	3	2	2	6
21	MS	1151573	41	38	28	3	13	139	130	118	9	21	3	3	2	5	5	4	6
22	SK	91953	59	58	46	1	13	99	99	98	0	1	5	5	5	4	4	4	6
23	KK	1538796	59	50	46	9	13	153	141	126	12	27	7	6	6	2	2	2	6
24	RS	74094	53	45	40	8	13	89	82	62	7	27	7	7	6	3	2	2	6
25	PG	1528192	53.2	50	40.2	3.2	13	95	88	82	7	13	3	3	3	3	3	3	6
26	AK	59642	41.9	37	28.9	4.9	13	66	56	39	10	27	7	7	6	5	5	4	6
27	HK	1762751	50	48	37	2	13	169	161	142	8	27	6	5	5	3	2	2	6
28	KS	71428	62	59	49	3	13	423	388	396	35	27	4	4	5	5	5	4	6
29	MH	52615	68	64	55	4	13	218	140	140	78	78	4	3	3	4	3	2	6
30	UR	1202853	50	95	37	-45	13	208	210	223	-2	-15	5	5	4	3	3	3	6
31	GS	831727	86	110	73	-24	13	198	243	207	-45	-9	5	5	5	3	2	2	6
32	CS	1442784	180	271	297	-91	-117	600	512	431	88	169	4	4	4	3	2	2	6
33	LD	37575	88	53	75	35	13	304	155	157	149	147	6	4	4	2	4	5	5
34	S	1488612	87	86	74	1	13	294	126	80	168	214	6	5	6	2	2	2	5
35	BK	1534840	25	35	42	-10	-17	78	69	65	9	13	5	5	4	3	3	3	6
36	BR	115718	192	279	297	-87	-105	167	158	154	9	13	5	6	5	5	5	4	6
37	GS	1695223	310	282	297	28	13	210	201	197	9	13	6	7	6	4	4	4	5
38	PS	93624	50	41	37	9	13	65	56	52	9	13	5	4	4	2	2	2	6
39	RG	1195183	120	100	107	20	13	160	151	147	9	13	3	3	2	4	4	4	6
40	GS	1529782	120	106	107	14	13	150	141	137	9	13	5	5	5	3	2	2	6
41	BS	1539625	69	60	56	9	13	112	103	99	9	13	7	6	6	5	5	4	6
42	GS	352125	180	179	167	1	13	81	72	68	9	13	7	7	6	4	4	4	6
43	SR	79111	190	210	277	-20	-87	149	160	136	-11	13	7	7	6	4	3	3	5
44	PS	1539699	35	30	22	5	13	78	72	65	6	13	6	5	5	2	2	2	3
45	BS	1653458	50	41	37	9	13	115	109	102	6	13	4	4	5	4	2	2	6
46	SS	296473	97	96	84	1	13	210	204	197	6	13	4	3	3	3	2	2	6
47	DS	156621	62	60	49	2	13	199	200	186	-1	13	5	5	4	5	5	4	4
48	J	1745061	44	40	31	4	13	120	106	107	14	13	5	5	5	2	2	2	4
49	JS	1762466	85	81	72	4	13	85	77	72	8	13	4	4	4	4	3	3	6
50	M	1421879	30	29	17	1	13	75	68	57	7	18	6	4	4	3	2	2	6

SR. NO	NAME	MRD . NO	REMOTE MEMORY WEEK 3	REMOTE MEMORY WEEK 16	RECENT MEMORY WEEK 1	RECENT MEMORY WEEK 3	RECENT MEMORY WEEK 16	MENTAL BALANCE WEEK 1	MENTAL BALANCE WEEK 3	MENTAL BALANCE WEEK 16	ATTENETION AND CONCENTRATIO	ATTENTION AND CONCENTRATION WEEK 3	ATTENTION AND CONCENTRATION WEEK 16	DELAYED RECALL WEEK 1	DELAYED RECALL WEEK 3	DELAYED RECALL WEEK 16	IMMEDIATE RECALL WEEK 1
1	RS	45720	5	5	5	5	5	6	6	6	9	9	9	7	8	9	12
2	S	135050	6	6	5	5	5	9	8	8	10	8	8	10	10	10	12
3	RK	99886	6	6	5	5	5	9	9	8	12	12	10	10	10	10	12
4	JK	850319	6	6	5	5	5	9	9	8	12	12	10	8	7	7	10
5	AD	1158930	6	6	5	5	5	6	6	6	9	9	9	10	10	9	11
6	RS	1759698	6	6	5	5	5	9	8	8	10	8	8	10	8	7	10
7	VK	62916	6	6	5	5	5	9	9	8	12	12	10	10	9	9	12
8	PK	1443712	6	6	5	5	5	9	9	8	12	12	10	10	10	10	12
9	RK	1634315	6	6	5	5	5	9	9	8	12	12	10	10	10	9	11
10	KS	1642409	6	6	5	5	5	9	9	8	12	12	10	10	10	9	11
11	M	1199536	6	6	5	5	5	6	6	6	9	9	9	8	7	7	10
12	GS	1541709	5	4	5	5	6	6	5	5	8	5	9	9	8	8	12
13	SB	37941	5	5	4	4	5	6	6	6	7	10	8	6	6	4	11
14	VL	38770	5	5	5	5	5	7	6	6	8	7	8	8	7	7	10
15	JS	74019	6	6	5	5	5	9	8	8	8	8	7	6	7	8	12
16	S	1049140	6	5	5	5	5	8	8	8	10	7	7	10	10	9	11
17	IS	1339870	5	5	4	4	5	6	6	6	7	10	10	9	8	8	12
18	JK	1132829	6	6	5	5	5	7	6	6	8	7	8	6	6	4	11
19	GS	199826	6	6	5	5	5	9	8	8	8	8	7	8	7	7	10
20	GK	1565812	6	6	5	5	5	9	8	8	10	8	8	10	10	9	11
21	MS	1151573	6	6	5	5	5	9	9	8	12	12	10	9	8	8	12
22	SK	91953	6	6	4	4	4	9	8	8	11	8	8	10	10	10	12
23	KK	1538796	6	6	4	4	4	5	5	4	7	7	7	7	8	8	9
24	RS	74094	6	6	4	4	4	9	8	8	11	8	8	10	10	9	11
25	PG	1528192	6	6	5	5	5	7	6	6	8	7	8	10	9	7	9
26	AK	59642	6	6	4	4	4	5	5	4	7	7	7	9	8	8	12
27	HK	1762751	6	6	4	4	4	9	8	8	11	8	8	10	10	9	11
28	KS	71428	6	6	4	4	4	5	5	4	7	7	7	9	8	8	12
29	MH	52615	6	6	5	5	5	8	8	6	8	7	6	7	8	9	12
30	UR	1202853	6	6	5	5	5	6	4	4	8	8	8	6	6	4	11
31	GS	831727	6	6	5	4	4	6	4	8	8	7	7	6	4	5	11
32	CS	1442784	5	4	5	5	5	8	8	6	8	7	6	9	10	9	11
33	LD	37575	5	5	4	4	5	6	6	6	7	10	10	10	9	10	12
34	S	1488612	5	5	5	5	5	7	6	6	8	7	8	10	8	6	12
35	BK	1534840	6	6	5	5	5	9	8	8	8	8	7	10	9	7	9
36	BR	115718	6	5	5	5	5	9	8	8	10	8	8	10	8	7	10
37	GS	1695223	5	5	5	5	5	9	9	8	12	12	10	10	9	9	12
38	PS	93624	6	6	4	4	4	9	8	8	11	8	8	10	10	10	12
39	RG	1195183	6	6	4	4	4	5	5	4	7	7	7	10	10	9	11
40	GS	1529782	6	6	4	4	4	9	8	8	11	8	8	10	10	9	11
41	BS	1539625	6	6	4	4	4	5	5	4	7	7	7	8	7	7	10
42	GS	352125	5	4	4	4	4	9	8	8	11	8	8	9	8	8	12
43	SR	79111	5	5	5	5	5	7	7	7	9	8	8	10	8	8	12
44	PS	1539699	3	3	5	5	5	6	6	6	9	9	9	7	8	9	12
45	BS	1653458	6	6	5	5	5	9	8	8	10	8	8	6	6	4	11
46	SS	296473	5	5	5	5	5	9	9	8	12	12	10	6	4	5	11
47	DS	156621	5	5	5	5	5	9	9	8	12	12	10	10	10	9	11
48	J	1745061	4	4	5	5	5	9	9	8	12	12	10	9	8	8	12
49	JS	1762466	6	5	5	5	5	9	9	8	12	12	10	10	8	8	12
50	M	1421879	6	6	5	5	5	6	6	6	9	9	9	10	10	10	12

SR. NO	NAME	MRD . NO	IMMEDIATE RECALL WEEK 3	IMMEDIATE RECALL WEEK 16	RETENTION FOR SIMILAR PAIRS WEEK 1	RETENTION FOR SIMILAR PAIRS WEEK 3	RETENTION FOR SIMLAR PAIRS WEEK 16	RETENTION FOR DISIMILAR PAIRS WEEK 1	RETENTION FOR DISIMILAR PAIRS WEEK 3	RETENTION FOR DISIMILAR PAIRS WEEK 16	VISUAL RETENTION WEEK 1	VISUAL RETENTION WEEK 3	VISUAL RETENTION WEEK 16	RECOGNITION WEEK 1	RETENTION WEEK 3	RECOGNITION WEEK 16
1	RS	45720	11	11	5	5	5	14	14	13	12	12	11	10	10	9
2	S	135050	12	12	5	5	5	15	15	15	13	13	12	10	10	10
3	RK	99886	12	12	5	5	5	14	14	15	12	13	12	10	10	10
4	JK	850319	9	9	3	3	4	7	7	6	8	8	5	7	7	7
5	AD	1158930	12	12	5	5	5	15	15	15	13	13	12	10	10	10
6	RS	1759698	9	9	5	5	5	12	9	9	8	8	7	8	8	8
7	VK	62916	11	11	5	5	5	14	14	13	12	12	11	10	10	9
8	PK	1443712	12	12	5	5	5	15	15	15	13	13	12	10	10	10
9	RK	1634315	12	12	5	5	5	14	14	15	12	13	12	10	10	10
10	KS	1642409	12	12	5	5	5	5	5	4	12	12	12	9	9	9
11	M	1199536	9	9	4	4	4	10	12	12	11	10	10	9	9	8
12	GS	1541709	12	10	5	5	5	10	9	12	12	12	11	8	7	7
13	SB	37941	11	11	3	3	4	7	7	6	8	8	5	7	7	7
14	VL	38770	9	9	4	4	4	10	12	12	11	10	10	9	9	8
15	JS	74019	11	10	5	5	5	5	5	4	12	12	12	9	9	9
16	S	1049140	12	11	5	5	4	13	11	9	12	12	11	9	9	9
17	IS	1339870	12	10	5	5	5	14	14	15	12	13	12	10	10	10
18	JK	1132829	11	11	3	3	4	7	7	6	8	8	5	7	7	7
19	GS	199826	9	9	5	5	5	15	15	15	13	13	12	10	10	10
20	GK	1565812	12	11	5	4	4	11	13	13	4	8	9	9	9	9
21	MS	1151573	12	10	5	5	5	8	10	11	11	13	13	9	10	10
22	SK	91953	12	12	5	5	5	13	14	13	12	12	12	9	10	10
23	KK	1538796	8	8	5	3	3	9	8	8	7	6	6	7	7	7
24	RS	74094	12	11	3	3	4	7	7	6	8	8	5	7	7	7
25	PG	1528192	11	11	5	4	4	11	13	13	4	8	9	9	9	9
26	AK	59642	12	10	5	4	4	11	13	13	8	8	9	9	9	9
27	HK	1762751	12	11	5	5	5	8	10	11	11	13	13	9	10	10
28	KS	71428	12	10	5	5	5	8	10	11	11	13	13	8	8	7
29	MH	52615	11	11	5	4	4	11	13	13	10	8	9	9	9	9
30	UR	1202853	11	11	5	5	5	8	10	11	11	13	13	9	10	10
31	GS	831727	11	11	5	5	5	6	14	11	12	13	12	9	10	10
32	CS	1442784	12	11	4	4	4	13	13	12	11	11	10	9	9	8
33	LD	37575	11	11	4	4	4	14	14	14	12	12	11	9	9	9
34	S	1488612	10	8	4	4	4	13	13	14	11	12	11	9	9	9
35	BK	1534840	11	11	2	2	3	6	6	5	7	7	4	6	6	6
36	BR	115718	9	9	4	4	4	14	14	14	12	12	11	9	9	9
37	GS	1695223	11	11	4	4	4	11	8	8	7	7	6	7	7	7
38	PS	93624	12	12	4	4	4	13	13	12	11	11	10	9	9	8
39	RG	1195183	12	12	4	4	4	14	14	14	12	12	11	9	9	9
40	GS	1529782	12	12	4	4	4	13	13	14	11	12	11	9	9	9
41	BS	1539625	9	9	4	4	4	4	4	3	11	11	11	8	8	8
42	GS	352125	12	10	3	3	3	9	11	11	10	9	9	8	8	7
43	SR	79111	10	10	4	4	4	9	8	-1	11	11	10	7	6	6
44	PS	1539699	11	11	2	2	3	6	6	5	7	7	4	6	6	6
45	BS	1653458	11	11	3	3	3	9	11	11	10	9	9	8	8	7
46	SS	296473	11	11	4	4	4	4	4	3	11	11	11	8	8	8
47	DS	156621	11	11	4	4	3	12	10	8	11	11	10	8	8	8
48	J	1745061	12	10	4	4	4	13	13	14	11	12	11	9	9	9
49	JS	1762466	10	10	2	2	3	6	6	5	7	7	4	6	6	6
50	M	1421879	12	12	4	4	4	14	14	14	12	12	11	9	9	9

SR. NO	NAME	MRD . NO	Total score of memory week1	Total score of memory week3	Total score of memory week16	Δ Total score of memory	Δ Total score of memory	DSST week1	DSST week3	DSST week16	Δ DSST week3	Δ DSST week3	NLR week 1	MLR week 1	PLR week 1	NLR Week 3	MLR Week3	PLR Week 3	NLR Week 16	MLR Week 16	PLR Week 16	Change NLR Week 3
1	RS	45720	93	88	85	5	8	29	26	18	3	11	5.24	0.69	144.12	3.12	0.67	141.72	4.61	0.72	144.29	2.12
2	S	135050	97	97	93	0	4	31	31	30	0	1	4.40	0.70	160.88	2.17	0.71	87.83	4.36	0.78	192.37	2.23
3	RK	99886	94	96	92	-2	2	52	52	55	0	-3	3.23	0.92	227.06	2.84	0.98	271.85	2.55	0.99	304.84	0.39
4	JK	850319	64	62	57	2	7	38	38	55	0	-17	3.12	0.76	59.04	2.80	0.83	224.43	2.73	0.67	106.80	0.32
5	AD	1158930	97	97	93	0	4	15	14	15	1	0	6.53	0.95	304.71	6.53	0.97	350.37	6.83	0.97	366.41	0.00
6	RS	1759698	94	96	92	-2	2	31	28	20	3	11	2.95	0.68	92.79	2.56	0.80	132.88	2.07	0.56	104.47	0.40
7	VK	62916	93	88	85	5	8	33	33	32	0	1	2.76	0.71	125.93	3.38	0.90	225.96	2.56	0.56	88.89	-0.62
8	PK	1443712	97	97	93	0	4	54	54	57	0	-3	2.83	0.60	118.19	3.63	0.58	161.65	2.04	0.72	157.98	-0.79
9	RK	1634315	94	96	92	-2	2	40	40	57	0	-17	2.75	0.71	200.53	2.05	0.66	145.23	3.15	0.98	474.23	0.69
10	KS	1642409	72	72	71	0	1	61	50	56	11	5	2.80	0.75	87.53	3.09	0.85	107.33	2.66	0.95	81.34	-0.29
11	M	1199536	76	74	74	2	2	16	15	15	1	1	4.21	0.66	284.43	2.25	0.62	64.28	3.50	0.83	259.64	1.96
12	GS	1541709	64	62	57	2	7	25	22	18	3	7	2.78	0.57	112.03	2.94	0.58	108.11	3.23	0.59	107.16	-0.16
13	SB	37941	64	62	57	2	7	34	34	33	0	1	3.72	0.76	176.21	2.71	0.74	158.50	2.11	0.63	106.24	1.01
14	VL	38770	76	74	74	2	2	51	57	55	-6	-4	5.06	0.60	172.98	2.13	0.66	285.29	1.90	0.63	88.79	2.93
15	JS	74019	72	72	71	0	1	50	50	46	0	4	3.31	0.60	56.95	1.83	0.62	69.49	2.68	0.63	86.10	1.47
16	S	1049140	83	79	78	4	5	19	20	22	-1	-3	5.95	0.94	216.29	5.95	0.94	232.39	7.35	0.99	294.00	0.00
17	IS	1339870	94	96	92	-2	2	45	35	34	10	11	5.73	0.81	132.95	3.26	0.74	135.00	3.65	0.69	89.86	2.47
18	JK	1132829	64	62	57	2	7	58	50	46	8	12	3.25	0.77	66.89	2.52	0.78	166.82	2.50	0.63	70.25	0.73
19	GS	199826	97	97	93	0	4	29	27	23	2	6	2.46	0.76	63.55	3.39	0.75	120.21	3.27	0.65	137.17	-0.93
20	GK	1565812	74	80	85	-6	-11	29	25	20	4	9	3.46	0.66	120.85	2.04	0.75	143.00	2.87	0.68	95.71	1.42
21	MS	1151573	76	74	74	2	2	29	27	22	2	7	3.47	0.63	86.24	3.42	0.74	177.26	2.86	0.64	117.22	0.04
22	SK	91953	89	89	88	0	1	34	34	33	0	1	4.15	0.68	136.02	2.48	0.59	163.60	3.57	0.73	121.56	1.67
23	KK	1538796	94	96	92	-2	2	26	23	15	3	11	4.34	0.87	104.76	2.69	0.73	121.23	3.92	0.71	166.56	1.65
24	RS	74094	64	62	57	2	7	28	28	27	0	1	3.06	0.70	122.33	3.49	0.77	163.58	2.10	0.65	153.39	-0.43
25	PG	1528192	74	80	85	-6	-11	24	24	23	0	1	3.42	0.68	289.63	2.85	0.79	202.08	3.25	0.91	278.66	0.56
26	AK	59642	93	88	85	5	8	49	49	52	0	-3	4.14	0.93	194.41	2.81	0.94	203.42	3.90	0.97	216.48	1.33
27	HK	1762751	97	97	93	0	4	35	35	52	0	-17	2.78	0.64	103.33	3.97	0.63	145.04	3.06	0.75	168.73	-1.18
28	KS	71428	76	74	74	2	2	32	31	32	1	0	3.82	0.72	93.52	2.34	0.68	78.30	4.05	0.76	190.37	1.48
29	MH	52615	75	79	78	-4	-3	28	25	17	3	11	4.17	0.74	149.14	4.40	3.23	213.58	3.21	0.72	114.39	-0.23
30	UR	1202853	63	61	56	2	7	30	30	29	0	1	3.42	0.68	165.70	2.15	0.68	172.03	2.70	0.64	213.80	1.27
31	GS	831727	63	61	56	2	7	51	51	54	0	-3	3.73	0.74	89.12	2.88	0.64	84.80	2.44	0.64	107.86	0.84
32	CS	1442784	92	87	84	5	8	17	17	20	0	-3	5.62	0.93	152.62	6.40	0.94	478.40	7.50	0.91	255.24	-0.78
33	LD	37575	96	96	92	0	4	28	25	23	3	5	2.92	0.61	66.58	1.72	0.81	186.38	3.57	0.85	192.41	1.20
34	S	1488612	93	95	91	-2	2	13	12	12	1	1	2.72	0.84	155.98	2.73	0.94	146.23	3.24	0.98	117.99	-0.01
35	BK	1534840	63	61	56	2	7	52	49	50	3	2	2.70	0.70	64.80	3.30	0.91	71.89	3.05	0.75	78.20	-0.60
36	BR	115718	96	96	92	0	4	11	13	15	-2	-4	5.10	1.33	359.68	3.48	0.73	233.05	2.86	0.62	105.50	1.62
37	GS	1695223	93	95	91	-2	2	28	24	42	4	-14	2.48	0.72	88.04	4.45	0.77	153.01	3.20	0.60	115.57	-1.97
38	PS	93624	92	87	84	5	8	17	17	23	0	-6	2.48	0.64	111.35	2.29	0.61	53.72	2.04	0.73	153.73	0.19
39	RG	1195183	96	96	92	0	4	26	27	29	-1	-3	3.06	0.58	139.74	2.77	0.66	107.85	3.63	0.64	111.23	0.28
40	GS	1529782	93	95	91	-2	2	42	32	31	10	11	2.65	0.63	139.28	2.57	0.61	85.23	2.19	0.78	221.29	0.08
41	BS	1539625	71	71	70	0	1	55	47	43	8	12	3.62	0.66	73.09	3.40	0.73	87.46	3.04	0.72	180.53	0.22
42	GS	352125	75	73	73	2	2	26	24	20	2	6	2.46	0.72	119.49	4.35	0.72	234.75	2.26	0.68	115.32	-1.89
43	SR	79111	63	61	56	2	7	16	18	20	-2	-4	5.29	0.77	181.84	5.71	0.73	163.70	7.79	0.83	242.09	-0.42
44	PS	1539699	63	61	56	2	7	26	24	19	2	7	3.32	0.61	108.93	2.65	0.64	101.62	3.45	0.68	141.65	0.66
45	BS	1653458	75	73	73	2	2	31	31	30	0	1	4.49	0.79	118.82	3.67	0.94	169.36	2.73	0.68	130.53	0.82
46	SS	296473	71	71	70	0	1	23	20	12	3	11	2.87	0.91	172.13	2.58	0.67	121.74	2.98	0.57	153.28	0.29
47	DS	156621	82	78	77	4	5	25	25	24	0	1	3.04	0.69	133.40	3.52	0.80	156.99	2.89	0.62	128.36	-0.48
48	J	1745061	93	95	91	-2	2	46	46	49	0	-3	3.72	0.59	99.94	3.01	0.60	145.55	2.80	0.62	66.62	0.71
49	JS	1762466	63	61	56	2	7	32	32	49	0	-17	3.57	0.61	77.37	2.95	0.68	139.36	2.99	0.61	135.36	0.62
50	M	1421879	96	96	92	0	4	29	28	29	1	0	2.64	0.59	118.54	4.07	0.73	93.01	2.32	0.74	150.76	-1.43

SR. NO	NAME	MRD . NO	Change MLR Week 3	Change PLR Week 3	Change NLR week 16	Change MLR week 16	Change PLR week 16	ABSOLUTE NEUTROPHIL COUNT WEEK 1	ABSOLUTE LYMPHOCYTE COUNT WEEK 1	ABSOLUTE MONOCYTE COUNT WEEK	PLATELET COUNT WEEK 1	WBC WEEK 1	ABSOLUTE NEUTROPHIL COUNT Week 3	ABSOLUTE LYMPHOCYTE COUNT Week 3	ABSOLUTE MONOCYTE COUNT Week	PLATELET COUNT Week 3	WBC Week 3	NLR Week 3
1	RS	45720	0.02	2.40	0.63	-0.04	-0.17	5.30	1.46	0.27	195.14	7.03	5.78	1.31	0.30	204.90	7.39	4.41
2	S	135050	-0.01	73.05	0.04	-0.08	-31.49	5.42	1.94	0.38	291.99	7.74	5.91	1.74	0.42	306.59	8.07	3.39
3	RK	99886	-0.06	-44.79	0.68	-0.07	-77.78	2.85	1.75	0.74	378.87	5.34	3.11	1.57	0.82	397.82	5.49	1.98
4	JK	850319	-0.07	-165.39	0.39	0.09	-47.76	4.91	3.23	0.84	158.49	8.98	5.35	2.91	0.93	166.41	9.19	1.84
5	AD	1158930	-0.02	-45.66	-0.30	-0.02	-61.70	5.42	1.10	0.82	324.36	7.35	5.92	0.99	0.90	340.57	7.81	5.97
6	RS	1759698	-0.12	-40.09	0.88	0.12	-11.67	3.67	2.71	0.50	224.34	6.87	4.00	2.44	0.55	235.55	6.99	1.64
7	VK	62916	-0.19	-100.03	0.20	0.15	37.03	3.83	3.29	0.70	381.10	7.82	4.18	2.96	0.77	400.15	7.91	1.41
8	PK	1443712	0.01	-43.46	0.79	-0.12	-39.79	4.48	3.63	0.35	392.76	8.47	4.89	3.27	0.39	412.40	8.55	1.50
9	RK	1634315	0.05	55.30	-0.40	-0.27	-273.70	2.32	2.03	0.42	386.07	4.77	2.53	1.82	0.46	405.37	4.82	1.39
10	KS	1642409	-0.10	-19.80	0.14	-0.20	6.19	4.15	3.46	0.87	268.55	8.48	4.53	3.12	0.96	281.98	8.60	1.45
11	M	1199536	0.04	220.15	0.71	-0.18	24.79	3.48	1.33	0.21	365.51	5.02	3.80	1.20	0.23	383.79	5.22	3.17
12	GS	1541709	-0.01	3.93	-0.45	-0.02	4.88	4.18	3.54	0.26	361.14	7.98	4.56	3.19	0.29	379.19	8.04	1.43
13	SB	37941	0.02	17.71	1.61	0.12	69.96	2.92	1.38	0.36	229.78	4.66	3.19	1.24	0.39	241.26	4.83	2.56
14	VL	38770	-0.06	-112.31	3.16	-0.02	84.19	7.59	2.19	0.22	357.23	10.00	8.28	1.97	0.24	375.09	10.49	4.20
15	JS	74019	-0.02	-12.54	0.62	-0.03	-29.15	5.79	3.39	0.34	159.25	9.52	6.32	3.05	0.37	167.21	9.74	2.07
16	S	1049140	0.00	-16.11	-1.40	-0.05	-77.72	6.31	1.45	0.64	299.07	8.40	6.88	1.30	0.70	314.02	8.89	5.27
17	IS	1339870	0.06	-2.06	2.09	0.12	43.09	6.97	1.69	0.52	207.50	9.18	7.61	1.52	0.57	217.88	9.70	5.01
18	JK	1132829	-0.01	-99.93	0.75	0.15	-3.36	5.22	3.17	0.87	180.14	9.25	5.69	2.85	0.96	189.15	9.50	2.00
19	GS	199826	0.01	-56.66	-0.80	0.10	-73.62	2.73	3.16	0.81	169.24	6.70	2.97	2.84	0.89	177.70	6.71	1.05
20	GK	1565812	-0.09	-22.14	0.59	-0.02	25.15	5.45	2.92	0.46	324.07	8.83	5.94	2.63	0.50	340.28	9.08	2.26
21	MS	1151573	-0.12	-91.02	0.61	-0.01	-30.98	5.75	3.08	0.39	234.97	9.23	6.27	2.77	0.43	246.72	9.48	2.26
22	SK	91953	0.09	-27.58	0.59	-0.04	14.46	6.71	2.63	0.48	331.19	9.82	7.32	2.37	0.53	347.75	10.22	3.09
23	KK	1538796	0.13	-16.47	0.43	0.15	-61.80	4.81	1.76	0.64	166.34	7.21	5.25	1.58	0.71	174.66	7.54	3.32
24	RS	74094	-0.07	-41.25	0.96	0.05	-31.06	2.97	2.04	0.40	228.82	5.41	3.24	1.83	0.44	240.26	5.52	1.77
25	PG	1528192	-0.11	87.55	0.17	-0.23	10.97	2.58	1.42	0.26	397.79	4.27	2.82	1.28	0.29	417.68	4.39	2.20
26	AK	59642	-0.01	-9.01	0.24	-0.04	-22.07	3.92	1.54	0.67	284.87	6.13	4.27	1.39	0.73	299.12	6.40	3.07
27	HK	1762751	0.01	-41.72	-0.28	-0.11	-65.41	4.40	3.73	0.51	347.68	8.63	4.80	3.35	0.56	365.06	8.71	1.43
28	KS	71428	0.04	15.22	-0.23	-0.04	-96.85	6.11	2.75	0.61	229.69	9.47	6.66	2.48	0.68	241.17	9.81	2.69
29	MH	52615	-2.49	-64.43	0.96	0.02	34.75	5.65	2.20	0.53	306.47	8.38	6.17	1.98	0.58	321.80	8.73	3.11
30	UR	1202853	-0.01	-6.33	0.73	0.04	-48.10	4.35	2.39	0.42	371.49	7.16	4.75	2.15	0.46	390.07	7.36	2.21
31	GS	831727	0.10	4.32	1.29	0.10	-18.74	8.17	3.84	0.91	303.97	12.92	8.91	3.46	1.00	319.16	13.37	2.58
32	CS	1442784	-0.01	-325.77	-1.88	0.02	-102.62	5.86	1.46	0.77	208.24	8.10	6.40	1.31	0.85	218.65	8.56	4.87
33	LD	37575	-0.20	-119.79	-0.65	-0.24	-125.83	3.64	2.76	0.31	156.10	6.70	3.97	2.48	0.34	163.91	6.78	1.60
34	S	1488612	-0.10	9.75	-0.52	-0.14	37.99	2.82	2.52	0.85	367.52	6.18	3.07	2.27	0.94	385.90	6.27	1.36
35	BK	1534840	-0.21	-7.09	-0.35	-0.05	-13.40	3.12	2.83	0.57	155.32	6.52	3.41	2.55	0.62	163.08	6.58	1.34
36	BR	115718	0.60	126.63	2.24	0.71	254.18	3.69	1.05	0.87	368.68	5.61	4.02	0.95	0.96	387.11	5.93	4.24
37	GS	1695223	-0.05	-64.96	-0.72	0.12	-27.53	3.17	3.62	0.80	282.23	7.59	3.46	3.25	0.88	296.35	7.60	1.06
38	PS	93624	0.03	57.64	0.44	-0.09	-42.37	3.33	3.80	0.52	384.77	7.64	3.63	3.42	0.57	404.01	7.62	1.06
39	RG	1195183	-0.08	31.88	-0.57	-0.06	28.51	3.92	2.70	0.22	349.70	6.84	4.28	2.43	0.24	367.18	6.95	1.76
40	GS	1529782	0.02	54.06	0.46	-0.15	-82.00	3.25	3.09	0.40	399.48	6.74	3.54	2.78	0.44	419.46	6.77	1.27
41	BS	1539625	-0.07	-14.37	0.58	-0.06	-107.44	7.63	3.77	0.61	237.68	12.00	8.32	3.39	0.67	249.56	12.38	2.45
42	GS	352125	0.00	-115.26	0.20	0.03	4.17	2.69	3.12	0.68	341.80	6.48	2.93	2.81	0.74	358.89	6.48	1.04
43	SR	79111	0.04	18.14	-2.50	-0.06	-60.25	5.37	1.46	0.39	250.48	7.22	5.86	1.31	0.43	263.01	7.61	4.47
44	PS	1539699	-0.03	7.31	-0.14	-0.06	-32.72	4.68	2.73	0.30	269.97	7.72	5.11	2.46	0.33	283.47	7.90	2.08
45	BS	1653458	-0.15	-50.54	1.76	0.11	-11.71	8.14	2.82	0.83	306.88	11.79	8.88	2.54	0.91	322.22	12.33	3.50
46	SS	296473	0.24	50.38	-0.11	0.35	18.84	2.88	2.27	0.94	368.42	6.09	3.14	2.05	1.03	386.84	6.22	1.54
47	DS	156621	-0.12	-23.60	0.15	0.07	5.04	4.61	3.21	0.59	396.02	8.41	5.03	2.89	0.65	415.82	8.57	1.74
48	J	1745061	-0.02	-45.61	0.92	-0.03	33.33	8.07	3.80	0.33	342.07	12.20	8.80	3.42	0.36	359.17	12.58	2.57
49	JS	1762466	-0.07	-61.99	0.58	0.00	-57.99	7.44	3.78	0.40	254.44	11.62	8.11	3.40	0.44	267.16	11.96	2.39
50	M	1421879	-0.14	25.52	0.31	-0.14	-32.22	7.14	2.35	0.21	255.34	9.71	7.79	2.12	0.24	268.11	10.15	3.68

SR. NO	NAME	MRD . NO	MLR Week 3	PLR Week 3	ABSOLUTE NEUTROPHIL COUNT WEEK 16	ABSOLUTE LYMPHOCYTE COUNT WEEK 16	ABSOLUTE MONOCYTE COUNT WEEK 16	PLATELET COUNT WEEK 16	WBC WEEK 16
1	RS	45720	0.23	156.47	6.26	1.16	0.33	214.66	7.75
2	S	135050	0.24	176.03	6.40	1.55	0.46	321.18	8.41
3	RK	99886	0.52	253.24	3.37	1.40	0.89	416.76	5.65
4	JK	850319	0.32	57.21	5.80	2.59	1.01	174.34	9.39
5	AD	1158930	0.91	343.83	6.41	0.88	0.99	356.79	8.28
6	RS	1759698	0.22	96.59	4.33	2.17	0.60	246.77	7.10
7	VK	62916	0.26	135.25	4.53	2.63	0.84	419.21	8.00
8	PK	1443712	0.12	126.22	5.30	2.90	0.42	432.04	8.63
9	RK	1634315	0.25	222.29	2.74	1.62	0.50	424.67	4.87
10	KS	1642409	0.31	90.45	4.90	2.77	1.05	295.41	8.72
11	M	1199536	0.19	320.17	4.11	1.07	0.25	402.06	5.43
12	GS	1541709	0.09	119.04	4.94	2.83	0.32	397.25	8.09
13	SB	37941	0.31	193.91	3.46	1.11	0.43	252.75	4.99
14	VL	38770	0.12	190.14	8.97	1.75	0.26	392.95	10.98
15	JS	74019	0.12	54.78	6.84	2.71	0.40	175.18	9.96
16	S	1049140	0.54	240.67	7.46	1.16	0.76	328.97	9.38
17	IS	1339870	0.37	143.44	8.24	1.35	0.62	228.25	10.21
18	JK	1132829	0.34	66.37	6.16	2.53	1.04	198.16	9.74
19	GS	199826	0.31	62.48	3.22	2.53	0.98	186.16	6.73
20	GK	1565812	0.19	129.33	6.44	2.34	0.55	356.48	9.33
21	MS	1151573	0.16	88.95	6.80	2.47	0.47	258.47	9.73
22	SK	91953	0.23	147.02	7.93	2.10	0.58	364.31	10.61
23	KK	1538796	0.45	110.55	5.69	1.40	0.77	182.97	7.86
24	RS	74094	0.24	131.05	3.51	1.63	0.48	251.70	5.62
25	PG	1528192	0.23	326.23	3.05	1.14	0.31	437.57	4.51
26	AK	59642	0.53	215.14	4.63	1.24	0.80	313.36	6.67
27	HK	1762751	0.17	108.88	5.20	2.98	0.61	382.45	8.78
28	KS	71428	0.27	97.44	7.22	2.20	0.74	252.66	10.16
29	MH	52615	0.29	162.34	6.68	1.76	0.63	337.12	9.08
30	UR	1202853	0.22	181.65	5.15	1.91	0.51	408.64	7.56
31	GS	831727	0.29	92.31	9.65	3.07	1.09	334.36	13.82
32	CS	1442784	0.65	166.40	6.93	1.17	0.93	229.06	9.03
33	LD	37575	0.14	66.02	4.30	2.21	0.37	171.71	6.87
34	S	1488612	0.41	170.31	3.33	2.01	1.02	404.28	6.36
35	BK	1534840	0.24	63.93	3.69	2.27	0.68	170.85	6.64
36	BR	115718	1.01	407.96	4.36	0.84	1.05	405.54	6.25
37	GS	1695223	0.27	91.05	3.75	2.89	0.96	310.46	7.60
38	PS	93624	0.17	118.24	3.93	3.04	0.62	423.24	7.59
39	RG	1195183	0.10	151.36	4.64	2.16	0.26	384.67	7.05
40	GS	1529782	0.16	150.83	3.84	2.47	0.48	439.43	6.79
41	BS	1539625	0.20	73.60	9.01	3.01	0.73	261.45	12.75
42	GS	352125	0.26	127.74	3.17	2.50	0.81	375.98	6.48
43	SR	79111	0.33	200.48	6.35	1.17	0.47	275.53	7.99
44	PS	1539699	0.14	115.42	5.53	2.18	0.37	296.97	8.08
45	BS	1653458	0.36	126.95	9.62	2.26	0.99	337.56	12.87
46	SS	296473	0.50	189.15	3.40	1.82	1.13	405.26	6.34
47	DS	156621	0.23	143.96	5.44	2.57	0.71	435.62	8.73
48	J	1745061	0.11	104.94	9.53	3.04	0.39	376.28	12.97
49	JS	1762466	0.13	78.60	8.79	3.02	0.49	279.89	12.29
50	M	1421879	0.11	126.63	8.44	1.88	0.26	280.87	10.58

SR. NO	NAME	MRD . NO	GROUP	AGE	SEX	MARITAL STATUS	EDUCATION	OCCUPATION	FAMILY TYPE	RELIGION	RESIDENCE	INCOME	DURATION OF ILLNESS (YEARS)	FAMILY HISTORY OF PSYCHIATRIC ILLNESS	MOOD STABILIZERS
51	RS	140637	CASES	65	MALE	MARRIED	MATRICULATION	SEMIPROFESSIONAL	NUCLEAR	SIKH	URBAN	20000	11	ABSENT	LITHIUM
52	JS	1434814	CASES	59	MALE	MARRIED	MATRICULATION	SEMISKILLED	NUCLEAR	SIKH	RURAL	60000	3	ABSENT	SODIUM VALPROATE
53	BK	1155357	CASES	53	FEMALE	MARRIED	MIDDLE SCHOL	UNEMPLOYED	NUCLEAR	SIKH	RURAL	90000	15	ABSENT	LITHIUM
54	JC	1502963	CASES	18	MALE	UNMARRIED	MATRICULATION	UNEMPLOYED	JOINT	SIKH	URBAN	18800	40	ABSENT	SODIUM VALPROATE
55	RS	79094	CASES	45	MALE	MARRIED	HIGHER SECONDARY	SEMISKILLED	JOINT	SIKH	RURAL	200000	21	ABSENT	SODIUM VALPROATE
56	R	78568	CASES	33	FEMALE	MARRIED	HIGHER SECONDARY	UNEMPLOYED	NUCLEAR	HINDU	URBAN	20000	17	ABSENT	LITHIUM
57	GS	1529782	CASES	34	MALE	MARRIED	PRIMARY	UNEMPLOYED	NUCLEAR	SIKH	URBAN	200000	5	ABSENT	SODIUM VALPROATE
58	PS	1076307	CASES	39	MALE	MARRIED	GRADUATION	SEMIPROFESSIONAL	NUCLEAR	ABSENT	URBAN	30000	5	ABSENT	LITHIUM
59	A	1572453	CASES	41	FEMALE	MARRIED	MATRICULATION	UNEMPLOYED	NUCLEAR	HINDU	URBAN	10000	8	ABSENT	LITHIUM
60	GK	68089	CASES	48	FEMALE	MARRIED	MATRICULATION	UNEMPLOYED	NUCLEAR	SIKH	RURAL	12000	38	ABSENT	LITHIUM
61	SD	506062	CASES	47	FEMALE	MARRIED	MATRICULATION	UNEMPLOYED	NUCLEAR	HINDU	URBAN	30000	17	ABSENT	LITHIUM
62	MS	1760170	CASES	39	MALE	MARRIED	GRADUATION	SEMIPROFESSIONAL	NUCLEAR	HINDU	URBAN	50000	2	ABSENT	LITHIUM
63	HS	151278	CASES	35	MALE	MARRIED	GRADUATION	SEMIPROFESSIONAL	NUCLEAR	SIKH	URBAN	40000	39	ABSENT	SODIUM VALPROATE
64	AS	1449169	CASES	35	MALE	MARRIED	HIGHER SECONDARY	SEMISKILLED	NUCLEAR	SIKH	RURAL	50000	7	ABSENT	SODIUM VALPROATE
65	SM	1452507	CASES	40	MALE	MARRIED	GRADUATION	SEMISKILLED	NUCLEAR	HINDU	RURAL	20000	12	ABSENT	LITHIUM
66	RS	1034935	CASES	64	MALE	MARRIED	GRADUATION	SEMISKILLED	NUCLEAR	SIKH	RURAL	30000	6	ABSENT	SODIUM VALPROATE
67	SS	1395241	CASES	29	MALE	UNMARRIED	GRADUATION	UNEMPLOYED	JOINT	SIKH	RURAL	15000	2	ABSENT	LITHIUM
68	PS	62913	CASES	63	MALE	MARRIED	PRIMARY	SEMISKILLED	NUCLEAR	SIKH	RURAL	40000	2	ABSENT	LITHIUM
69	DS	1461849	CASES	47	MALE	MARRIED	HIGHER SECONDARY	SEMISKILLED	NUCLEAR	SIKH	RURAL	100000	20	ABSENT	SODIUM VALPROATE
70	SK	74209	CASES	48	MALE	MARRIED	GRADUATION	SEMIPROFESSIONAL	NUCLEAR	HINDU	URBAN	80000	10	ABSENT	LITHIUM
71	AK	213687	CASES	37	MALE	MARRIED	HIGHER SECONDARY	PROFESSIONAL	NUCLEAR	HINDU	URBAN	25000	7	ABSENT	LITHIUM
72	GS	1185205	CASES	37	MALE	MARRIED	GRADUATION	SEMISKILLED	JOINT	SIKH	RURAL	70000	3	ABSENT	SODIUM VALPROATE
73	GS	1656892	CASES	20	MALE	UNMARRIED	HIGHER SECONDARY	UNEMPLOYED	NUCLEAR	SIKH	URBAN	20000	0	ABSENT	SODIUM VALPROATE
74	PK	1528192	CASES	39	FEMALE	MARRIED	GRADUATION	UNEMPLOYED	NUCLEAR	HINDU	URBAN	60000	12	ABSENT	LITHIUM
75	KS	1442680	CASES	54	MALE	MARRIED	PRIMARY	UNEMPLOYED	NUCLEAR	SIKH	RURAL	25000	20	ABSENT	LITHIUM
76	JP	176632	CASES	50	MALE	MARRIED	GRADUATION	SEMISKILLED	NUCLEAR	SIKH	RURAL	48000	15	PRESENT	SODIUM VALPROATE
77	SR	1242469	CASES	59	FEMALE	MARRIED	HIGHER SECONDARY	UNEMPLOYED	NUCLEAR	HINDU	URBAN	70000	37	ABSENT	LITHIUM
78	GS	1702934	CASES	30	MALE	MARRIED	GRADUATION	SEMIPROFESSIONAL	JOINT	SIKH	URBAN	150000	5	PRESENT	SODIUM VALPROATE
79	PP	1730388	CASES	35	MALE	MARRIED	GRADUATION	PROFESSIONAL	NUCLEAR	SIKH	RURAL	450000	8	ABSENT	LITHIUM
80	SK	1722635	CASES	40	MALE	MARRIED	MATRICULATION	SEMISKILLED	NUCLEAR	HINDU	URBAN	27000	2	PRESENT	SODIUM VALPROATE
81	MS	852809	CASES	20	MALE	UNMARRIED	HIGHER SECONDARY	UNEMPLOYED	NUCLEAR	SIKH	URBAN	90000	0.2	PRESENT	SODIUM VALPROATE
82	M	1727509	CASES	39	FEMALE	MARRIED	POST-GRADUATE	PROFESSIONAL	NUCLEAR	HINDU	URBAN	70000	31	ABSENT	LITHIUM
83	T	506552	CASES	24	FEMALE	UNMARRIED	POST-GRADUATE	PROFESSIONAL	NUCLEAR	HINDU	URBAN	42000	3	ABSENT	LITHIUM
84	AP	1725141	CASES	18	MALE	UNMARRIED	HIGHER SECONDARY	UNEMPLOYED	NUCLEAR	SIKH	RURAL	29900	0.4	PRESENT	SODIUM VALPROATE
85	R	539022	CASES	46	FEMALE	MARRIED	GRADUATION	UNEMPLOYED	NUCLEAR	HINDU	URBAN	43000	8	ABSENT	LITHIUM
86	M	1723628	CASES	30	FEMALE	MARRIED	GRADUATION	PROFESSIONAL	JOINT	HINDU	URBAN	30000	3	PRESENT	LITHIUM
87	D	1250127	CASES	23	MALE	UNMARRIED	GRADUATION	UNEMPLOYED	JOINT	HINDU	URBAN	42000	31	PRESENT	SODIUM VALPROATE
88	H	950495	CASES	43	MALE	MARRIED	MATRICULATION	UNSKILLED	NUCLEAR	SIKH	RURAL	12000	18	ABSENT	SODIUM VALPROATE
89	T	1193762	CASES	33	MALE	MARRIED	POST-GRADUATE	SEMIPROFESSIONAL	NUCLEAR	HINDU	URBAN	90000	10	PRESENT	LITHIUM
90	RN	1606866	CASES	29	MALE	UNMARRIED	HIGHER SECONDARY	SEMISKILLED	NUCLEAR	HINDU	URBAN	21000	5	ABSENT	LITHIUM
91	AS	17010135	CASES	60	MALE	MARRIED	MATRICULATION	UNEMPLOYED	NUCLEAR	SIKH	URBAN	38000	30	ABSENT	SODIUM VALPROATE
92	HS	426042	CASES	55	MALE	MARRIED	HIGHER SECONDARY	UNEMPLOYED	NUCLEAR	SIKH	URBAN	56000	30	ABSENT	LITHIUM
93	PS	1709907	CASES	34	MALE	MARRIED	POST-GRADUATE	SEMIPROFESSIONAL	NUCLEAR	HINDU	URBAN	44000	9	PRESENT	LITHIUM
94	PK	1705694	CASES	52	FEMALE	MARRIED	HIGHER SECONDARY	UNEMPLOYED	JOINT	SIKH	URBAN	200000	30	PRESENT	LITHIUM
95	HS	1004901	CASES	31	MALE	UNMARRIED	GRADUATION	PROFESSIONAL	NUCLEAR	HINDU	RURAL	18000	0.2	PRESENT	SODIUM VALPROATE
96	JK	1562277	CASES	30	FEMALE	UNMARRIED	GRADUATION	PROFESSIONAL	NUCLEAR	SIKH	RURAL	33000	4	PRESENT	LITHIUM
97	SY	1253284	CASES	44	MALE	MARRIED	GRADUATION	SEMISKILLED	NUCLEAR	HINDU	URBAN	20000	10	PRESENT	SODIUM VALPROATE
98	P	1196517	CASES	58	MALE	MARRIED	MATRICULATION	SEMISKILLED	JOINT	HINDU	URBAN	19000	20	ABSENT	LITHIUM
99	A	1189011	CASES	34	FEMALE	MARRIED	HIGHER SECONDARY	UNEMPLOYED	JOINT	HINDU	URBAN	22000	32	ABSENT	LITHIUM
100	V	847469	CASES	69	MALE	MARRIED	MATRICULATION	UNEMPLOYED	NUCLEAR	HINDU	URBAN	21000	2	ABSENT	SODIUM VALPROATE

SR. NO	NAME	MRD . NO	TMTA week 1	TMTA week 3	TMTA week 16	Δ TMTA week 3	Δ TMTA week 16	TMTB week 1	TMTB week 3	TMTB week 16	Δ TMTB week 3	Δ TMTB week 16	DIGIT FORWARD WEEK 1	DIGIT FORWARD WEEK 3	DIGIT FORWARD WEEK 16	DIGIT BACKWARD WEEK 1	DIGIT BACKWARD WEEK 3	DIGIT BACKWARD WEEK 16	REMOTE MEMORY WEEK 1
51	RS	140637	93	88	80	5	13	178	164	155	14	23	3	4	3	5	5	4	5
52	JS	1434814	103	101	90	2	13	185	171	162	14	23	8	7	6	4	4	4	6
53	BK	1155357	116	97	103	19	13	120	106	97	14	23	4	4	4	3	2	2	6
54	JC	1502963	124.6	220	281.6	-95.4	-157	48	34	25	14	23	5	4	4	5	5	4	6
55	RS	79094	40	33	27	7	13	52	38	29	14	23	3	3	2	4	4	4	6
56	R	78568	52	52	39	0	13	123	123	125	0	-2	5	5	5	2	2	2	6
57	GS	1529782	51	45	38	6	13	87	85	78	2	9	4	3	3	3	2	2	5
58	PS	1076307	55.3	51	42.3	4.3	13	88	77	73	11	15	4	4	4	5	5	4	3
59	A	1572453	45	41	32	4	13	55	44	40	11	15	4	4	4	3	2	2	6
60	GK	68089	152	250	293	-98	-141	63	52	48	11	15	5	5	5	5	5	4	6
61	SD	506062	25.1	25	12.1	0.1	13	48	37	33	11	15	6	6	6	4	3	2	4
62	MS	1760170	36.2	36	23.2	0.2	13	70	59	55	11	15	6	6	6	3	3	3	4
63	HS	151278	190	252	274	-62	-84	120	109	105	11	15	6	6	6	3	2	2	6
64	AS	1449169	59	55	46	4	13	121	110	106	11	15	5	5	5	2	4	5	5
65	SM	1452507	120	110	107	10	13	190	179	175	11	15	4	4	4	2	2	2	4
66	RS	1034935	24.9	20	11.9	4.9	13	75	64	60	11	15	4	4	4	3	3	3	5
67	SS	1395241	35.4	34	22.4	1.4	13	70	59	55	11	15	4	4	4	5	5	4	6
68	PS	62913	70	75	57	-5	13	160	162	165	-2	-5	4	4	4	4	4	4	6
69	DS	1461849	25	17	12	8	13	64	57	51	7	13	5	5	5	2	2	2	5
70	SK	74209	27	20	14	7	13	52	45	39	7	13	4	4	4	4	4	4	6
71	AK	213687	24	25	11	-1	13	76	69	63	7	13	5	5	5	5	5	4	6
72	GS	1185205	26	20	13	6	13	54	47	41	7	13	5	5	5	5	5	4	6
73	GS	1656892	26	20	13	6	13	52	45	39	7	13	6	6	6	5	5	4	6
74	PK	1528192	53.2	50	40.2	3.2	13	95	88	82	7	13	3	3	3	3	3	3	6
75	KS	1442680	26	23	13	3	13	90	83	77	7	13	6	6	6	4	4	3	6
76	JP	176632	40	41	39	-1	1	100	90	90	10	10	5	5	5	4	5	5	6
77	SR	1242469	150	251	294	-101	-144	120	121	128	-1	-8	5	5	4	4	4	3	6
78	GS	1702934	35	34	30	1	5	70	65	65	5	5	6	6	6	4	5	5	5
79	PP	1730388	40	39	38	1	2	60	61	61	-1	-1	5	5	4	4	4	4	6
80	SK	1722635	50	48	47	2	3	110	110	109	0	1	4	4	4	3	3	3	5
81	MS	852809	30	30	29	0	1	60	59	57	1	3	6	6	6	5	5	5	6
82	M	1727509	131	233	285	-102	-154	59	60	62	-1	-3	6	6	6	5	5	4	6
83	T	506552	35	36	37	-1	-2	49	51	51	-2	-2	5	5	5	5	4	4	6
84	AP	1725141	40	37	36	3	4	100	101	98	-1	2	6	6	6	4	5	5	5
85	R	539022	50	52	53	-2	-3	130	132	154	-2	-24	6	6	5	4	3	3	6
86	M	1723628	38	39	40	-1	-2	80	81	81	-1	-1	6	6	6	5	5	4	6
87	D	1250127	141	240	283	-99	-142	68	68	65	0	3	6	6	7	5	5	5	6
88	H	950495	51	51	50	0	1	141	140	138	1	3	5	5	5	4	4	5	5
89	T	1193762	45	46	49	-1	-4	110	111	111	-1	-1	5	5	5	4	4	3	6
90	RN	1606866	55	55	57	0	-2	109	109	110	0	-1	5	5	4	4	4	4	6
91	AS	17010135	59	59	58	0	1	140	140	138	0	2	4	4	4	3	4	4	6
92	HS	426042	44	44	43	0	1	126	126	128	0	-2	5	5	4	4	4	4	6
93	PS	1709907	39	40	40	-1	-1	80	84	85	-4	-5	6	6	5	5	5	5	6
94	PK	1705694	150	250	273	-100	-123	86	86	89	0	-3	6	5	5	4	4	3	6
95	HS	1004901	42	43	41	-1	1	88	86	86	2	2	5	5	5	4	4	4	6
96	JK	1562277	39	39	40	0	-1	44	45	48	-1	-4	6	6	5	4	4	4	6
97	SY	1253284	49	49	48	0	1	80	80	78	0	2	4	4	4	3	4	4	6
98	P	1196517	48	50	50	-2	-2	100	100	102	0	-2	5	5	5	4	4	3	6
99	A	1189011	134	234	273	-100	-139	56	56	58	0	-2	5	5	5	4	4	3	6
100	V	847469	44	44	41	0	3	98	98	96	0	2	6	6	6	4	4	5	6

SR. NO	NAME	MRD . NO	REMOTE MEMORY WEEK 3	REMOTE MEMORY WEEK 16	RECENT MEMORY WEEK 1	RECENT MEMORY WEEK 3	RECENT MEMORY WEEK 16	MENTAL BALANCE WEEK 1	MENTAL BALANCE WEEK 3	MENTAL BALANCE WEEK 16	ATTENETION AND CONCENTRATIO	ATTENTION AND CONCENTRATION WEEK 3	ATTENTION AND CONCENTRATION WEEK 16	DELAYED RECALL WEEK 1	DELAYED RECALL WEEK 3	DELAYED RECALL WEEK 16	IMMEDIATE RECALL WEEK 1
51	RS	140637	5	5	5	5	5	6	5	5	8	5	6	6	4	5	11
52	JS	1434814	6	6	4	4	5	6	6	6	7	10	9	9	10	9	11
53	BK	1155357	6	6	5	5	5	7	6	6	8	7	8	10	10	9	11
54	JC	1502963	6	6	5	5	5	9	8	8	8	8	7	10	10	9	11
55	RS	79094	6	6	5	5	5	8	8	8	10	7	7	10	8	8	12
56	R	78568	5	4	4	4	5	6	6	6	7	10	9	9	9	9	10
57	GS	1529782	5	5	5	5	5	7	6	6	8	7	8	6	8	8	10
58	PS	1076307	3	3	5	5	5	9	8	8	8	8	7	7	8	8	9
59	A	1572453	6	6	5	5	5	9	8	8	10	8	8	10	10	9	11
60	GK	68089	5	5	5	5	5	9	9	8	12	12	10	9	8	8	12
61	SD	506062	5	5	4	4	4	9	8	8	11	8	8	10	10	9	11
62	MS	1760170	4	4	4	4	4	5	5	4	7	7	7	9	8	8	12
63	HS	151278	6	5	4	4	4	9	8	8	11	8	8	7	8	9	12
64	AS	1449169	5	5	4	4	4	5	5	4	7	7	7	6	6	4	11
65	SM	1452507	4	4	4	4	4	9	8	8	11	8	8	10	10	10	12
66	RS	1034935	5	5	4	4	4	5	5	4	7	7	7	6	4	5	11
67	SS	1395241	6	6	5	5	5	8	8	6	8	7	6	9	10	9	11
68	PS	62913	6	6	5	5	5	6	4	4	8	8	8	6	6	5	10
69	DS	1461849	5	5	5	4	5	6	4	4	8	8	8	6	6	4	11
70	SK	74209	6	6	5	5	5	8	8	6	8	7	6	6	4	5	11
71	AK	213687	6	6	4	4	5	6	6	6	7	10	9	9	10	9	11
72	GS	1185205	6	6	5	5	5	7	6	6	8	7	8	10	9	10	12
73	GS	1656892	6	6	5	5	5	9	8	8	8	8	7	10	8	6	12
74	PK	1528192	6	6	5	5	5	7	6	6	8	7	8	10	9	7	9
75	KS	1442680	6	6	5	5	5	9	8	8	8	8	7	10	8	7	10
76	JP	176632	6	6	4	4	5	6	6	6	7	10	12	7	8	8	9
77	SR	1242469	6	6	5	4	4	7	6	6	9	9	7	8	8	7	7
78	GS	1702934	8	6	6	6	8	8	8	10	11	11	9	9	9	8	9
79	PP	1730388	6	6	6	6	5	9	8	8	9	9	8	8	8	7	9
80	SK	1722635	5	5	5	5	6	7	7	8	7	7	7	7	7	7	8
81	MS	852809	6	6	5	5	5	8	9	9	11	11	11	9	9	10	11
82	M	1727509	6	6	5	5	4	8	8	7	11	11	10	8	8	7	10
83	T	506552	6	6	5	5	4	8	8	7	10	9	9	8	8	7	11
84	AP	1725141	5	6	4	5	5	9	9	9	10	11	11	9	9	10	11
85	R	539022	6	6	5	5	4	9	8	8	7	10	9	9	9	8	11
86	M	1723628	6	6	5	5	4	7	7	6	11	11	10	10	10	9	12
87	D	1250127	6	6	5	5	5	7	7	8	11	11	12	9	9	10	12
88	H	950495	5	6	5	5	5	7	7	8	9	9	10	7	7	8	10
89	T	1193762	6	6	5	5	5	9	9	8	9	9	8	9	9	8	13
90	RN	1606866	6	6	5	4	4	7	7	6	9	9	8	8	8	7	10
91	AS	17010135	6	6	4	5	5	7	7	7	8	8	7	8	8	9	11
92	HS	426042	6	5	4	4	4	7	7	6	9	9	8	8	7	7	9
93	PS	1709907	6	6	5	5	4	8	8	8	11	11	10	9	9	8	11
94	PK	1705694	6	6	5	5	5	8	8	7	10	9	8	9	9	9	11
95	HS	1004901	6	6	5	5	5	9	9	9	9	9	9	9	9	10	13
96	JK	1562277	6	6	5	5	4	8	8	8	10	10	9	10	10	10	13
97	SY	1253284	6	6	4	4	5	7	7	8	7	8	8	8	8	7	12
98	P	1196517	6	6	5	5	4	7	7	6	9	9	8	9	9	9	9
99	A	1189011	6	6	5	5	5	7	7	6	9	9	8	9	9	8	11
100	V	847469	6	6	5	5	4	7	7	6	10	10	11	8	8	9	9

SR. NO	NAME	MRD . NO	IMMEDIATE RECALL WEEK 3	IMMEDIATE RECALL WEEK 16	RETENTION FOR SIMILAR PAIRS WEEK 1	RETENTION FOR SIMILAR PAIRS WEEK 3	RETENTION FOR SIMLAR PAIRS WEEK 16	RETENTION FOR DISIMILAR PAIRS WEEK 1	RETENTION FOR DISIMILAR PAIRS WEEK 3	RETENTION FOR DISIMILAR PAIRS WEEK 16	VISUAL RETENTION WEEK 1	VISUAL RETENTION WEEK 3	VISUAL RETENTION WEEK 16	RECOGNITION WEEK 1	RETENTION WEEK 3	RECOGNITION WEEK 16
51	RS	140637	11	11	4	3	3	10	12	12	10	9	9	8	8	8
52	JS	1434814	12	11	4	4	4	7	9	10	10	12	12	8	9	9
53	BK	1155357	12	12	4	4	4	12	13	12	11	11	11	8	9	9
54	JC	1502963	12	12	4	2	2	8	7	7	8	8	7	6	6	6
55	RS	79094	10	10	2	2	3	6	6	5	7	7	6	6	6	6
56	R	78568	10	12	4	3	3	10	12	12	9	7	8	8	8	8
57	GS	1529782	11	12	5	5	5	14	14	15	12	13	12	10	10	10
58	PS	1076307	8	8	3	3	4	7	7	6	8	8	5	7	7	7
59	A	1572453	12	11	5	5	5	15	15	15	13	13	12	10	10	10
60	GK	68089	12	10	5	5	5	12	9	9	8	8	7	8	8	8
61	SD	506062	12	11	5	5	5	14	14	13	12	12	11	10	10	9
62	MS	1760170	12	10	5	5	5	15	15	15	13	13	12	10	10	10
63	HS	151278	11	11	5	5	5	14	14	15	12	13	12	10	10	10
64	AS	1449169	11	11	5	5	5	5	5	4	12	12	12	9	9	9
65	SM	1452507	12	12	4	4	4	10	12	12	11	10	10	9	9	8
66	RS	1034935	11	11	5	5	5	10	9	9	12	12	11	8	7	7
67	SS	1395241	12	11	3	3	4	7	7	6	8	8	5	7	7	7
68	PS	62913	10	9	4	4	4	10	12	12	11	10	10	9	9	8
69	DS	1461849	11	11	5	5	5	5	5	4	12	12	12	9	9	9
70	SK	74209	11	11	5	5	4	13	11	9	12	12	11	9	9	9
71	AK	213687	12	11	5	5	5	14	14	15	12	13	12	10	10	10
72	GS	1185205	11	11	3	3	4	7	7	6	8	8	5	7	7	7
73	GS	1656892	10	8	5	5	5	15	15	15	13	13	12	10	10	10
74	PK	1528192	11	11	5	4	4	11	13	13	4	8	9	9	9	9
75	KS	1442680	9	9	5	5	5	8	10	11	11	13	13	9	10	10
76	JP	176632	8	8	5	5	5	13	14	13	12	12	12	9	10	10
77	SR	1242469	7	7	5	5	4	12	12	11	11	11	10	8	8	7
78	GS	1702934	9	9	5	5	5	13	13	14	11	11	11	10	10	10
79	PP	1730388	9	8	5	5	4	13	12	12	10	10	10	9	9	8
80	SK	1722635	8	9	5	5	5	12	12	13	9	9	10	9	9	10
81	MS	852809	11	12	5	5	5	12	12	13	11	12	12	9	9	10
82	M	1727509	10	10	5	5	4	12	12	11	11	11	10	9	8	8
83	T	506552	11	10	5	5	4	13	12	12	11	11	10	10	10	9
84	AP	1725141	11	12	5	5	5	13	13	13	11	11	12	10	10	10
85	R	539022	10	10	5	5	4	13	13	12	13	12	12	9	9	8
86	M	1723628	12	11	5	5	5	12	12	11	13	13	12	10	9	9
87	D	1250127	12	12	5	5	5	12	12	13	13	13	13	10	10	10
88	H	950495	11	12	5	5	5	9	9	11	10	11	11	7	7	9
89	T	1193762	13	12	5	5	5	13	13	12	10	10	10	9	9	9
90	RN	1606866	10	9	5	4	4	10	8	9	9	9	8	7	7	7
91	AS	17010135	11	12	5	5	5	11	11	12	8	9	9	7	7	8
92	HS	426042	9	8	5	5	4	10	10	9	9	9	8	8	8	7
93	PS	1709907	11	11	5	5	5	13	13	12	12	12	11	9	9	10
94	PK	1705694	11	10	5	5	4	13	12	12	12	12	12	10	9	9
95	HS	1004901	13	12	5	5	5	13	13	13	12	12	12	9	9	10
96	JK	1562277	13	12	5	5	4	12	12	11	12	12	11	9	9	9
97	SY	1253284	12	13	4	5	5	11	11	11	11	11	12	8	8	9
98	P	1196517	8	8	5	5	5	11	11	10	11	11	10	9	9	8
99	A	1189011	11	10	5	5	5	12	12	11	11	11	10	9	9	9
100	V	847469	9	10	5	5	5	11	11	12	11	11	11	9	9	9

SR. NO	NAME	MRD . NO	Total score of memory week1	Total score of memory week3	Total score of memory week16	Δ Total score of memory	Δ Total score of memory	DSST week1	DSST week3	DSST week16	Δ DSST week3	Δ DSST week3	NLR week 1	MLR week 1	PLR week 1	NLR Week 3	MLR Week3	PLR Week 3	NLR Week 16	MLR Week 16	PLR Week 16	Change NLR Week 3
51	RS	140637	73	79	84	-6	-11	25	22	14	3	11	4.41	0.96	259.60	3.97	0.96	408.07	3.53	0.94	445.81	0.44
52	JS	1434814	75	73	73	2	2	27	27	26	0	1	2.42	0.57	63.03	2.52	0.70	84.29	2.55	0.70	120.46	-0.10
53	BK	1155357	88	88	87	0	1	48	48	51	0	-3	3.38	0.68	60.51	5.27	0.76	201.39	6.06	0.66	120.61	-1.89
54	JC	1502963	93	95	91	-2	2	14	14	16	0	-2	5.27	0.80	183.70	2.62	0.75	113.22	2.73	0.75	99.43	2.65
55	RS	79094	63	61	56	2	7	25	22	20	3	5	3.08	0.66	68.95	1.75	0.81	104.88	2.70	0.73	150.38	1.33
56	R	78568	92	87	84	5	8	10	9	9	1	1	3.17	0.69	72.08	2.55	0.69	153.46	3.98	0.70	132.31	0.62
57	GS	1529782	94	96	92	-2	2	19	16	12	3	7	3.12	0.82	91.52	1.85	0.65	92.43	3.66	0.75	98.50	1.27
58	PS	1076307	64	62	57	2	7	28	28	27	0	1	4.07	0.63	67.87	4.86	0.85	281.27	7.38	0.60	93.14	-0.79
59	A	1572453	97	97	93	0	4	25	21	39	4	-14	3.12	0.59	80.31	2.74	0.74	99.28	3.53	0.75	246.74	0.37
60	GK	68089	94	96	92	-2	2	14	14	16	0	-2	5.17	0.76	350.92	4.37	0.87	365.18	4.94	0.73	395.14	0.80
61	SD	506062	93	88	85	5	8	23	24	26	-1	-3	3.98	0.94	138.11	3.70	0.84	166.31	3.68	0.94	126.11	0.28
62	MS	1760170	97	97	93	0	4	39	29	28	10	11	3.15	0.75	82.20	2.59	0.83	105.29	2.91	0.64	107.67	0.55
63	HS	151278	94	96	92	-2	2	12	14	18	-2	-6	5.22	1.14	325.53	4.31	0.63	186.28	3.81	0.72	162.42	0.91
64	AS	1449169	72	72	71	0	1	43	51	57	-8	-14	3.05	0.83	112.26	1.72	0.76	266.54	2.72	0.67	84.80	1.32
65	SM	1452507	76	74	74	2	2	23	19	14	4	9	4.29	0.82	186.57	5.23	0.77	305.40	6.16	0.78	150.76	-0.95
66	RS	1034935	80	76	75	4	5	23	21	16	2	7	3.11	0.63	142.68	3.25	0.62	133.67	2.78	0.59	116.39	-0.14
67	SS	1395241	81	82	73	-1	8	28	28	27	0	1	3.12	0.74	55.84	2.58	0.94	235.46	3.41	0.98	142.51	0.54
68	PS	62913	83	82	79	1	4	40	47	49	-7	-9	3.14	0.75	134.76	2.99	0.83	94.22	2.44	0.63	87.86	0.15
69	DS	1461849	79	76	74	3	5	22	22	21	0	1	4.10	0.74	191.19	3.94	0.98	444.83	4.45	0.67	184.89	0.16
70	SK	74209	91	86	80	5	11	43	43	46	0	-3	3.29	0.68	130.21	2.37	0.78	105.62	2.91	0.65	122.90	0.92
71	AK	213687	94	100	97	-6	-3	29	29	46	0	-17	2.67	0.60	123.23	3.38	0.75	107.57	3.15	0.60	91.71	-0.71
72	GS	1185205	83	79	77	4	6	26	25	26	1	0	4.13	0.69	191.23	4.68	0.69	176.15	2.80	0.58	104.52	-0.55
73	GS	1656892	104	99	92	5	12	22	19	11	3	11	2.88	0.82	91.35	3.60	0.74	157.16	3.13	0.71	147.07	-0.72
74	PK	1528192	80	84	84	-4	-4	24	24	23	0	1	3.42	0.68	289.63	4.06	0.72	387.04	5.21	0.72	421.90	-0.64
75	KS	1442680	91	92	90	-1	1	45	45	48	0	-3	6.96	0.93	145.97	7.49	0.93	134.52	7.52	0.93	157.60	-0.53
76	JP	176632	87	93	95	-6	-8	31	31	48	0	-17	3.26	0.65	164.58	2.28	0.66	85.52	3.28	0.55	121.94	0.98
77	SR	1242469	87	85	76	2	11	14	13	16	1	-2	4.75	0.72	148.43	6.56	0.70	143.57	7.15	0.61	102.69	-1.81
78	GS	1702934	97	101	101	-4	-4	41	43	45	-2	-4	2.60	0.61	90.63	2.50	0.73	110.05	1.80	0.62	90.36	0.10
79	PP	1730388	93	91	84	2	9	52	50	49	2	3	4.63	0.72	143.28	3.37	0.75	136.00	4.79	0.62	114.03	1.26
80	SK	1722635	81	81	87	0	-6	34	37	38	-3	-4	4.08	0.77	85.74	2.81	0.89	89.06	3.83	0.81	145.44	1.27
81	MS	852809	98	100	104	-2	-6	65	66	67	-1	-2	3.60	0.65	77.02	3.24	0.64	109.14	3.72	0.68	96.79	0.37
82	M	1727509	96	95	87	1	9	13	16	18	-3	-5	6.46	0.80	207.37	7.58	0.82	273.07	7.04	0.91	289.06	-1.12
83	T	506552	97	94	87	3	10	56	54	50	2	6	3.17	0.69	75.74	5.72	0.79	169.74	3.93	0.74	146.99	-2.55
84	AP	1725141	97	100	104	-3	-7	34	26	37	8	-3	4.41	0.95	234.82	2.53	0.63	118.80	2.11	0.58	121.39	1.88
85	R	539022	97	96	89	1	8	42	44	45	-2	-3	3.61	0.73	71.17	4.85	0.84	139.91	6.28	0.66	78.99	-1.24
86	M	1723628	102	101	93	1	9	65	64	63	1	2	6.60	0.82	123.74	7.52	0.91	148.49	7.38	0.91	152.33	-0.92
87	D	1250127	101	101	106	0	-5	10	11	16	-1	-6	5.18	0.66	184.82	2.80	0.80	107.61	2.70	0.65	134.58	2.38
88	H	950495	83	85	95	-2	-12	33	34	36	-1	-3	3.95	0.68	305.33	3.16	0.64	116.03	2.63	0.59	114.21	0.79
89	T	1193762	97	97	91	0	6	65	65	60	0	5	3.26	0.60	105.71	4.06	0.67	157.85	3.77	0.67	186.28	-0.80
90	RN	1606866	85	81	76	4	9	20	19	19	1	1	4.74	0.76	169.07	5.84	0.82	139.11	7.41	0.64	158.22	-1.10
91	AS	17010135	82	85	88	-3	-6	40	41	41	-1	-1	2.78	0.59	79.44	3.53	0.65	153.96	3.41	0.70	174.12	-0.75
92	HS	426042	84	83	74	1	10	30	30	29	0	1	3.77	0.98	217.34	5.22	0.98	222.51	3.93	0.87	192.37	-1.45
93	PS	1709907	100	100	95	0	5	40	41	41	-1	-1	3.66	0.70	114.48	3.15	0.69	110.65	5.13	0.63	172.15	0.51
94	PK	1705694	99	95	90	4	9	15	16	18	-1	-3	5.08	0.78	208.81	6.33	0.71	308.46	6.76	0.65	174.31	-1.25
95	HS	1004901	99	99	100	0	-1	25	29	30	-4	-5	3.57	0.71	61.02	2.33	0.73	101.67	3.11	0.75	107.64	1.24
96	JK	1562277	100	100	93	0	7	37	38	39	-1	-2	3.49	0.67	229.11	2.19	0.79	273.55	4.24	0.71	309.46	1.29
97	SY	1253284	85	88	92	-3	-7	28	29	30	-1	-2	6.06	0.66	141.11	1.92	0.64	115.03	3.53	0.63	114.28	4.14
98	P	1196517	90	89	82	1	8	19	19	18	0	1	4.68	0.97	195.60	3.60	0.97	150.37	3.83	0.94	166.41	1.08
99	A	1189011	93	93	86	0	7	16	16	18	0	-2	6.53	0.85	304.71	3.44	0.99	337.87	5.56	0.97	408.67	3.09
100	V	847469	91	91	94	0	-3	27	27	29	0	-2	2.92	0.74	127.64	3.04	0.75	208.67	2.90	0.73	187.87	-0.12

SR. NO	NAME	MRD . NO	Change MLR Week 3	Change PLR Week 3	Change NLR week 16	Change MLR week 16	Change PLR week 16	ABSOLUTE NEUTROPHIL COUNT WEEK 1	ABSOLUTE LYMPHOCYTE COUNT WEEK 1	ABSOLUTE MONOCYTE COUNT WEEK	PLATELET COUNT WEEK 1	WBC WEEK 1	ABSOLUTE NEUTROPHIL COUNT Week 3	ABSOLUTE LYMPHOCYTE COUNT Week 3	ABSOLUTE MONOCYTE COUNT Week	PLATELET COUNT Week 3	WBC Week 3	NLR Week 3
51	RS	140637	0.00	-148.46	0.88	0.02	-186.21	3.76	1.34	0.89	334.40	5.99	4.10	1.21	0.97	351.12	6.28	3.40
52	JS	1434814	-0.13	-21.26	-0.13	-0.13	-57.43	3.23	3.95	0.29	209.69	7.48	3.53	3.56	0.32	220.18	7.40	0.99
53	BK	1155357	-0.08	-140.88	-2.68	0.02	-60.10	6.25	3.52	0.63	177.62	10.39	6.81	3.17	0.70	186.50	10.67	2.15
54	JC	1502963	0.04	70.47	2.54	0.05	84.27	7.82	1.37	0.41	238.66	9.60	8.53	1.24	0.45	250.59	10.22	6.90
55	RS	79094	-0.14	-35.92	0.38	-0.07	-81.43	5.57	3.76	0.62	221.81	9.95	6.07	3.39	0.68	232.90	10.14	1.79
56	R	78568	0.00	-81.39	-0.82	-0.01	-60.24	5.66	3.61	0.69	224.08	9.96	6.17	3.25	0.76	235.28	10.18	1.90
57	GS	1529782	0.17	-0.91	-0.53	0.07	-6.98	3.89	2.56	0.82	208.40	7.27	4.25	2.30	0.90	218.82	7.45	1.85
58	PS	1076307	-0.22	-213.40	-3.31	0.02	-25.27	6.86	2.77	0.35	160.52	9.98	7.48	2.50	0.39	168.55	10.37	3.00
59	A	1572453	-0.15	-18.97	-0.41	-0.15	-166.43	3.33	2.20	0.21	154.47	5.74	3.63	1.98	0.23	162.19	5.84	1.84
60	GK	68089	-0.11	-14.26	0.23	0.03	-44.22	4.16	1.16	0.30	396.93	5.63	4.54	1.05	0.33	416.78	5.92	4.33
61	SD	506062	0.10	-28.19	0.30	0.00	12.01	4.77	2.01	0.88	256.94	7.65	5.21	1.81	0.96	269.79	7.98	2.89
62	MS	1760170	-0.08	-23.10	0.24	0.11	-25.47	5.27	3.41	0.86	246.08	9.54	5.75	3.07	0.94	258.39	9.76	1.87
63	HS	151278	0.51	139.25	1.40	0.42	163.11	3.67	1.01	0.65	319.91	5.33	4.00	0.91	0.71	335.91	5.63	4.38
64	AS	1449169	0.07	-154.28	0.32	0.15	27.45	2.89	2.00	0.65	204.56	5.55	3.16	1.80	0.72	214.79	5.67	1.75
65	SM	1452507	0.04	-118.83	-1.87	0.04	35.81	5.89	2.19	0.70	387.49	8.79	6.43	1.98	0.77	406.86	9.17	3.26
66	RS	1034935	0.01	9.01	0.33	0.03	26.29	3.95	2.61	0.33	346.59	6.89	4.30	2.35	0.36	363.92	7.02	1.83
67	SS	1395241	-0.20	-179.62	-0.29	-0.24	-86.67	5.72	3.76	0.89	172.35	10.36	6.24	3.38	0.97	180.97	10.59	1.84
68	PS	62913	-0.08	40.54	0.70	0.12	46.90	3.13	2.04	0.51	254.40	5.69	3.42	1.84	0.57	267.11	5.82	1.86
69	DS	1461849	-0.24	-253.64	-0.35	0.07	6.30	5.11	2.04	0.49	369.78	7.64	5.58	1.84	0.54	388.27	7.95	3.04
70	SK	74209	-0.10	24.59	0.38	0.03	7.32	5.42	3.21	0.59	386.18	9.22	5.92	2.89	0.65	405.49	9.45	2.05
71	AK	213687	-0.16	15.66	-0.48	0.00	31.52	2.51	2.36	0.24	266.85	5.11	2.74	2.12	0.26	280.19	5.12	1.29
72	GS	1185205	0.00	15.09	1.33	0.12	86.72	4.24	1.67	0.32	303.35	6.23	4.62	1.51	0.36	318.52	6.49	3.07
73	GS	1656892	0.08	-65.82	-0.25	0.11	-55.72	3.01	2.36	0.75	191.76	6.12	3.29	2.12	0.83	201.35	6.24	1.55
74	PK	1528192	-0.04	-97.42	-1.79	-0.04	-132.27	2.58	1.42	0.26	397.79	4.27	2.82	1.28	0.29	417.68	4.39	2.20
75	KS	1442680	0.00	11.45	-0.56	0.00	-11.63	8.19	1.53	0.65	207.92	10.37	8.93	1.38	0.72	218.31	11.03	6.49
76	JP	176632	-0.01	79.06	-0.02	0.11	42.63	4.15	2.50	0.38	385.68	7.03	4.53	2.25	0.42	404.97	7.20	2.02
77	SR	1242469	0.01	4.86	-2.40	0.10	45.74	7.10	2.26	0.49	312.41	9.85	7.75	2.03	0.54	328.03	10.32	3.81
78	GS	1702934	-0.11	-19.42	0.80	-0.01	0.27	3.74	3.74	0.42	301.93	7.90	4.08	3.37	0.46	317.03	7.91	1.21
79	PP	1730388	-0.03	7.28	-0.16	0.10	29.24	6.32	2.09	0.47	278.17	8.88	6.90	1.88	0.51	292.08	9.29	3.67
80	SK	1722635	-0.12	-3.32	0.25	-0.04	-59.70	6.80	2.74	0.74	207.67	10.28	7.42	2.47	0.81	218.05	10.70	3.01
81	MS	852809	0.01	-32.13	-0.12	-0.03	-19.77	5.80	2.90	0.42	194.13	9.12	6.33	2.61	0.47	203.84	9.40	2.43
82	M	1727509	-0.02	-65.70	-0.58	-0.11	-81.70	5.05	1.04	0.62	205.12	6.72	5.51	0.94	0.69	215.38	7.14	5.89
83	T	506552	-0.10	-93.99	-0.76	-0.05	-71.25	4.69	2.99	0.56	196.61	8.24	5.12	2.69	0.61	206.44	8.42	1.90
84	AP	1725141	0.33	116.01	2.30	0.37	113.43	4.31	1.53	0.70	344.90	6.54	4.70	1.38	0.77	362.14	6.85	3.41
85	R	539022	-0.11	-68.74	-2.67	0.08	-7.82	7.82	3.88	0.90	237.53	12.61	8.53	3.49	0.99	249.41	13.02	2.44
86	M	1723628	-0.09	-24.75	-0.78	-0.09	-28.59	7.23	1.45	0.75	164.46	9.42	7.88	1.30	0.82	172.68	10.01	6.06
87	D	1250127	-0.14	77.21	2.48	0.01	50.24	8.04	2.24	0.36	392.28	10.64	8.77	2.02	0.40	411.89	11.19	4.34
88	H	950495	0.04	189.30	1.32	0.09	191.12	2.95	1.26	0.22	370.95	4.43	3.22	1.13	0.25	389.49	4.60	2.85
89	T	1193762	-0.07	-52.14	-0.51	-0.07	-80.57	6.62	3.99	0.40	381.94	11.01	7.22	3.59	0.44	401.03	11.25	2.01
90	RN	1606866	-0.07	29.97	-2.67	0.12	10.85	7.88	2.51	0.65	398.73	11.03	8.59	2.26	0.71	418.66	11.56	3.81
91	AS	17010135	-0.06	-74.52	-0.62	-0.12	-94.68	3.30	2.79	0.24	193.47	6.32	3.60	2.51	0.26	203.15	6.37	1.43
92	HS	426042	0.00	-5.17	-0.16	0.10	24.97	2.60	1.20	0.57	249.06	4.38	2.84	1.08	0.63	261.51	4.55	2.63
93	PS	1709907	0.01	3.84	-1.47	0.07	-57.67	6.68	3.25	0.65	339.56	10.58	7.29	2.92	0.71	356.54	10.93	2.49
94	PK	1705694	0.06	-99.65	-1.68	0.13	34.50	5.68	1.63	0.45	324.01	7.76	6.19	1.47	0.50	340.21	8.15	4.22
95	HS	1004901	-0.02	-40.65	0.47	-0.04	-46.62	7.29	3.69	0.78	188.47	11.77	7.96	3.32	0.86	197.90	12.14	2.39
96	JK	1562277	-0.11	-44.44	-0.75	-0.04	-80.34	3.05	1.62	0.28	353.96	4.94	3.32	1.45	0.31	371.66	5.08	2.29
97	SY	1253284	0.02	26.08	2.53	0.03	26.83	7.01	1.57	0.26	206.11	8.84	7.65	1.41	0.28	216.42	9.35	5.41
98	P	1196517	0.00	45.23	0.85	0.03	29.20	3.42	1.11	0.75	205.95	5.28	3.73	1.00	0.82	216.25	5.55	3.74
99	A	1189011	-0.14	-33.16	0.97	-0.12	-103.96	5.42	1.10	0.82	324.36	7.35	5.92	0.99	0.90	340.57	7.81	5.97
100	V	847469	-0.01	-81.03	0.02	0.01	-60.23	3.19	2.42	0.57	284.24	6.18	3.48	2.17	0.63	298.46	6.28	1.60

SR. NO	NAME	MRD . NO	MLR Week 3	PLR Week 3	ABSOLUTE NEUTROPHIL COUNT WEEK 16	ABSOLUTE LYMPHOCYTE COUNT WEEK 16	ABSOLUTE MONOCYTE COUNT WEEK 16	PLATELET COUNT WEEK 16	WBC WEEK 16
51	RS	140637	0.81	291.20	4.44	1.07	1.06	367.84	6.58
52	JS	1434814	0.09	61.86	3.82	3.16	0.35	230.66	7.33
53	BK	1155357	0.22	58.93	7.38	2.81	0.76	195.38	10.95
54	JC	1502963	0.36	202.64	9.25	1.10	0.49	262.52	10.83
55	RS	79094	0.20	68.78	6.58	3.01	0.74	243.99	10.33
56	R	78568	0.23	72.42	6.69	2.89	0.83	246.48	10.40
57	GS	1529782	0.39	95.10	4.60	2.05	0.99	229.24	7.63
58	PS	1076307	0.16	67.52	8.10	2.22	0.43	176.58	10.75
59	A	1572453	0.12	82.03	3.94	1.76	0.25	169.92	5.94
60	GK	68089	0.32	397.74	4.91	0.93	0.36	436.62	6.21
61	SD	506062	0.53	149.47	5.64	1.60	1.05	282.64	8.30
62	MS	1760170	0.31	84.23	6.23	2.73	1.03	270.69	9.98
63	HS	151278	0.78	368.12	4.33	0.81	0.78	351.90	5.92
64	AS	1449169	0.40	119.30	3.42	1.60	0.78	225.02	5.80
65	SM	1452507	0.39	206.00	6.97	1.76	0.84	426.24	9.56
66	RS	1034935	0.16	154.79	4.66	2.09	0.40	381.24	7.15
67	SS	1395241	0.29	53.48	6.76	3.01	1.06	189.59	10.83
68	PS	62913	0.31	145.56	3.70	1.63	0.62	279.83	5.95
69	DS	1461849	0.29	211.39	6.04	1.63	0.58	406.76	8.26
70	SK	74209	0.22	140.25	6.41	2.57	0.71	424.80	9.69
71	AK	213687	0.12	132.10	2.97	1.89	0.28	293.54	5.14
72	GS	1185205	0.24	211.44	5.01	1.34	0.39	333.69	6.74
73	GS	1656892	0.39	94.90	3.56	1.89	0.90	210.93	6.35
74	PK	1528192	0.23	326.23	3.05	1.14	0.31	437.57	4.51
75	KS	1442680	0.52	158.63	9.68	1.22	0.78	228.71	11.68
76	JP	176632	0.19	180.34	4.90	2.00	0.46	424.25	7.36
77	SR	1242469	0.27	161.50	8.39	1.81	0.59	343.65	10.79
78	GS	1702934	0.14	94.07	4.42	3.00	0.50	332.13	7.92
79	PP	1730388	0.27	155.49	7.47	1.67	0.56	305.99	9.70
80	SK	1722635	0.33	88.37	8.04	2.19	0.89	228.43	11.12
81	MS	852809	0.18	78.19	6.86	2.32	0.51	213.55	9.68
82	M	1727509	0.73	230.26	5.97	0.83	0.75	225.63	7.55
83	T	506552	0.23	76.70	5.54	2.39	0.67	216.27	8.61
84	AP	1725141	0.56	262.29	5.09	1.23	0.84	379.39	7.16
85	R	539022	0.28	71.36	9.25	3.11	1.08	261.28	13.44
86	M	1723628	0.63	132.69	8.54	1.16	0.90	180.91	10.60
87	D	1250127	0.20	203.96	9.50	1.80	0.43	431.50	11.73
88	H	950495	0.22	344.55	3.49	1.00	0.27	408.04	4.76
89	T	1193762	0.12	111.66	7.83	3.19	0.48	420.13	11.49
90	RN	1606866	0.32	185.58	9.31	2.01	0.78	438.60	12.09
91	AS	17010135	0.10	81.01	3.90	2.23	0.29	212.82	6.41
92	HS	426042	0.58	241.89	3.08	0.96	0.69	273.97	4.72
93	PS	1709907	0.24	121.90	7.90	2.60	0.78	373.52	11.28
94	PK	1705694	0.34	231.95	6.71	1.30	0.54	356.41	8.55
95	HS	1004901	0.26	59.52	8.62	2.96	0.93	207.32	12.51
96	JK	1562277	0.21	255.63	3.60	1.29	0.34	389.35	5.23
97	SY	1253284	0.20	152.96	8.29	1.26	0.31	226.72	9.85
98	P	1196517	0.82	216.54	4.04	0.89	0.90	226.55	5.82
99	A	1189011	0.91	343.83	6.41	0.88	0.99	356.79	8.28
100	V	847469	0.29	137.25	3.77	1.93	0.69	312.67	6.39

SR. NO	NAME	MRD . NO	GROUP	AGE	SEX	MARITAL STATUS	EDUCATION	OCCUPATION	FAMILY TYPE	RELIGION	RESIDENCE	INCOME	DURATION OF ILLNESS (YEARS)	FAMILY HISTORY OF PSYCHIATRIC ILLNESS	MOOD STABILIZERS
1	AG	1598651	CONTROL	38	FEMALE	MARRIED	MATRICULATION	PROFESSIONAL	NUCLEAR	HINDU	URBAN	30000	-	ABSENT	-
2	B	1604836	CONTROL	60	MALE	MARRIED	GRADUATION	UNEMPLOYED	NUCLEAR	HINDU	URBAN	28000	-	ABSENT	-
3	SS	1605668	CONTROL	27	MALE	UNMARRIED	GRADUATION	SEMISKILLED	JOINT	SIKH	RURAL	30000	-	PRESENT	-
4	MK	1604881	CONTROL	50	FEMALE	MARRIED	POST-GRADUATE	SEMIPROFESSIONAL	NUCLEAR	SIKH	RURAL	11000	-	PRESENT	-
5	MK	1604888	CONTROL	45	MALE	MARRIED	HIGHER SECONDARY	UNEMPLOYED	NUCLEAR	HINDU	URBAN	20000	-	PRESENT	-
6	AS	1604890	CONTROL	45	MALE	MARRIED	HIGHER SECONDARY	PROFESSIONAL	JOINT	HINDU	URBAN	28000	-	PRESENT	-
7	HM	1604370	CONTROL	26	MALE	UNMARRIED	MATRICULATION	SEMISKILLED	NUCLEAR	HINDU	URBAN	29000	-	ABSENT	-
8	B	1605578	CONTROL	46	MALE	MARRIED	GRADUATION	SEMIPROFESSIONAL	NUCLEAR	HINDU	RURAL	31000	-	ABSENT	-
9	TS	1604517	CONTROL	51	MALE	MARRIED	POST-GRADUATE	UNEMPLOYED	NUCLEAR	SIKH	RURAL	100000	-	ABSENT	-
10	CS	1604553	CONTROL	25	MALE	UNMARRIED	GRADUATION	PROFESSIONAL	NUCLEAR	HINDU	RURAL	200000	-	ABSENT	-
11	SK	1603881	CONTROL	36	MALE	MARRIED	GRADUATION	SKILLED WORKER	NUCLEAR	SIKH	RURAL	33000	-	PRESENT	-
12	SK	1604742	CONTROL	54	FEMALE	MARRIED	HIGHER SECONDARY	SEMISKILLED	NUCLEAR	SIKH	RURAL	24000	-	PRESENT	-
13	KV	1605516	CONTROL	37	FEMALE	MARRIED	HIGHER SECONDARY	UNSKILLED	NUCLEAR	HINDU	URBAN	12000	-	PRESENT	-
14	JS	1605519	CONTROL	26	MALE	UNMARRIED	POST-GRADUATE	PROFESSIONAL	JOINT	SIKH	RURAL	44000	-	ABSENT	-
15	KK	1605441	CONTROL	39	MALE	MARRIED	GRADUATION	SEMIPROFESSIONAL	NUCLEAR	HINDU	RURAL	76000	-	ABSENT	-
16	J	1605090	CONTROL	48	MALE	MARRIED	HIGHER SECONDARY	SEMISKILLED	NUCLEAR	HINDU	RURAL	88990	-	ABSENT	-
17	GS	1605448	CONTROL	32	MALE	MARRIED	HIGHER SECONDARY	UNEMPLOYED	NUCLEAR	SIKH	URBAN	80000	-	ABSENT	-
18	AS	1605574	CONTROL	42	FEMALE	MARRIED	GRADUATION	SKILLED WORKER	NUCLEAR	HINDU	URBAN	98000	-	ABSENT	-
19	RKS	1604942	CONTROL	25	FEMALE	UNMARRIED	HIGHER SECONDARY	UNEMPLOYED	NUCLEAR	HINDU	RURAL	40000	-	PRESENT	-
20	P	1605190	CONTROL	48	MALE	MARRIED	MATRICULATION	UNEMPLOYED	NUCLEAR	HINDU	URBAN	150000	-	ABSENT	-
21	DG	1604846	CONTROL	26	MALE	MARRIED	PRIMARY	SKILLED WORKER	NUCLEAR	HINDU	URBAN	80000	-	ABSENT	-
22	HS	1605241	CONTROL	45	MALE	MARRIED	PRIMARY	SEMISKILLED	NUCLEAR	HINDU	URBAN	80000	-	ABSENT	-
23	SG	1605323	CONTROL	47	MALE	MARRIED	HIGHER SECONDARY	PROFESSIONAL	NUCLEAR	ABSENT	URBAN	78000	-	PRESENT	-
24	V	1605206	CONTROL	55	FEMALE	MARRIED	HIGHER SECONDARY	SEMIPROFESSIONAL	JOINT	HINDU	URBAN	90000	-	PRESENT	-
25	AK	1605549	CONTROL	25	FEMALE	UNMARRIED	GRADUATION	UNEMPLOYED	JOINT	SIKH	URBAN	87000	-	ABSENT	-
26	AT	1605433	CONTROL	48	FEMALE	MARRIED	POST-GRADUATE	PROFESSIONAL	JOINT	SIKH	URBAN	20000	-	ABSENT	-
27	JK	1605412	CONTROL	47	MALE	MARRIED	GRADUATION	SEMISKILLED	NUCLEAR	SIKH	RURAL	12000	-	ABSENT	-
28	SS	1602353	CONTROL	56	MALE	MARRIED	POST-GRADUATE	UNSKILLED	NUCLEAR	HINDU	RURAL	23000	-	ABSENT	-
29	SK	1605312	CONTROL	36	FEMALE	MARRIED	HIGHER SECONDARY	UNEMPLOYED	NUCLEAR	HINDU	URBAN	9000	-	PRESENT	-
30	A	1608039	CONTROL	45	MALE	MARRIED	MATRICULATION	UNEMPLOYED	JOINT	HINDU	URBAN	17000	-	PRESENT	-

SR. NO	NAME	MRD . NO	TMTA week 1	TMTA week 3	TMTA week 16	Δ TMTA week 3	Δ TMTA week 16	TMTB week 1	TMTB week 3	TMTB week 16	Δ TMTB week 3	Δ TMTB week 16	DIGIT FORWARD WEEK 1	DIGIT FORWARD WEEK 3	DIGIT FORWARD WEEK 16	DIGIT BACKWARD WEEK 1	DIGIT BACKWARD WEEK 3	DIGIT BACKWARD WEEK 16	REMOTE MEMORY WEEK 1
1	AG	1598651	37	36	37	1	0	60	65	63	-5	-3	6	6	7	3	4	4	6
2	B	1604836	13	15	15	-2	-2	142	140	130	2	12	8	7	8	7	6	6	6
3	SS	1605668	26	26	26	0	0	69	72	75	-3	-6	7	7	7	5	5	5	5
4	MK	1604881	47	40	42	7	5	126	110	115	16	11	6	7	7	4	4	5	6
5	MK	1604888	17	19	18	-2	-1	47	49	52	-2	-5	7	7	7	5	5	5	5
6	AS	1604890	28	29	30	-1	-2	60	64	60	-4	0	7	8	7	7	7	6	6
7	HM	1604370	24	24	22	0	2	38	38	38	0	0	6	7	7	5	5	5	5
8	B	1605578	33	35	35	-2	-2	93	86	90	7	3	7	7	7	5	5	5	6
9	TS	1604517	40	40	40	0	0	65	60	62	5	3	6	7	7	6	6	4	6
10	CS	1604553	40	39	41	1	-1	70	71	70	-1	0	7	7	7	5	5	5	5
11	SK	1603881	30	29	29	1	1	48	49	49	-1	-1	7	8	8	6	6	7	6
12	SK	1604742	42	42	42	0	0	120	121	121	-1	-1	5	4	5	4	5	5	6
13	KV	1605516	30	30	28	0	2	50	50	50	0	0	6	5	5	5	5	5	6
14	JS	1605519	29	29	28	0	1	72	70	70	2	2	8	7	7	7	7	7	5
15	KK	1605441	35	35	34	0	1	77	75	75	2	2	5	5	6	5	5	6	6
16	J	1605090	25	25	24	0	1	56	56	56	0	0	6	6	6	5	5	5	6
17	GS	1605448	30	30	30	0	0	48	48	48	0	0	6	6	7	6	6	6	6
18	AS	1605574	30	28	27	2	3	55	55	55	0	0	7	7	6	7	7	6	5
19	RKS	1604942	40	40	39	0	1	80	80	80	0	0	8	7	7	7	7	7	6
20	P	1605190	35	35	34	0	1	62	62	62	0	0	7	7	7	5	5	5	5
21	DG	1604846	30	28	27	2	3	49	49	49	0	0	6	6	6	5	5	5	6
22	HS	1605241	30	29	29	1	1	60	60	60	0	0	7	7	7	6	6	6	6
23	SG	1605323	21	21	21	0	0	48	48	47	0	1	7	7	7	5	5	5	6
24	V	1605206	28	28	28	0	0	48	46	47	2	1	6	6	6	6	6	6	6
25	AK	1605549	29	29	29	0	0	48	48	47	0	1	6	6	6	5	5	5	5
26	AT	1605433	29	28	28	1	1	37	37	37	0	0	5	5	5	5	5	5	6
27	JK	1605412	30	30	30	0	0	39	38	38	1	1	7	7	6	5	5	5	6
28	SS	1602353	31	31	31	0	0	39	39	39	0	0	6	6	6	6	6	6	5
29	SK	1605312	32	32	32	0	0	50	50	50	0	0	7	7	7	6	6	6	6
30	A	1608039	40	38	38	2	2	60	58	58	2	2	6	6	6	7	7	7	6

SR. NO	NAME	MRD . NO	REMOTE MEMORY WEEK 3	REMOTE MEMORY WEEK 16	RECENT MEMORY WEEK 1	RECENT MEMORY WEEK 3	RECENT MEMORY WEEK 16	MENTAL BALANCE WEEK 1	MENTAL BALANCE WEEK 3	MENTAL BALANCE WEEK 16	ATTENETION AND CONCENTRATIO	ATTENTION AND CONCENTRATION WEEK 3	ATTENTION AND CONCENTRATION WEEK 16	DELAYED RECALL WEEK 1	DELAYED RECALL WEEK 3	DELAYED RECALL WEEK 16	IMMEDIATE RECALL WEEK 1
1	AG	1598651	6	6	5	5	4	8	6	6	9	10	11	10	10	10	12
2	B	1604836	6	6	5	5	5	8	8	9	15	13	14	10	9	10	12
3	SS	1605668	5	5	5	5	5	7	7	7	12	12	12	10	10	10	11
4	MK	1604881	6	6	5	5	5	7	7	7	10	11	12	10	10	10	10
5	MK	1604888	5	5	5	5	5	7	7	7	12	11	12	9	9	10	12
6	AS	1604890	6	6	4	5	5	9	8	8	14	15	13	10	10	10	12
7	HM	1604370	5	5	5	5	5	7	7	7	11	12	12	9	9	10	12
8	B	1605578	6	6	5	5	5	7	7	7	12	12	12	10	10	10	12
9	TS	1604517	6	6	5	5	5	7	7	7	13	13	11	9	9	10	10
10	CS	1604553	5	5	4	4	4	7	7	7	12	12	12	10	9	10	11
11	SK	1603881	6	6	5	4	5	9	8	8	13	14	15	9	10	9	12
12	SK	1604742	6	6	5	5	5	8	9	9	9	9	10	9	10	9	12
13	KV	1605516	6	6	5	5	5	7	7	7	11	10	10	10	10	10	12
14	JS	1605519	5	5	5	5	5	7	6	6	15	14	14	9	9	9	11
15	KK	1605441	6	6	6	5	5	7	7	7	10	10	12	9	10	10	12
16	J	1605090	6	6	6	5	5	9	9	9	11	10	10	10	9	10	12
17	GS	1605448	6	6	5	5	5	7	7	7	12	12	13	10	10	10	12
18	AS	1605574	5	5	5	5	5	9	9	9	14	14	12	9	10	10	12
19	RKS	1604942	6	6	5	5	5	9	8	8	15	14	14	10	10	10	12
20	P	1605190	5	5	5	5	5	8	9	9	12	12	12	10	10	10	12
21	DG	1604846	6	6	5	5	5	7	7	7	11	11	11	9	10	10	12
22	HS	1605241	6	6	5	5	5	9	9	9	13	13	13	10	10	10	12
23	SG	1605323	6	6	5	5	5	7	7	7	12	12	12	10	10	10	12
24	V	1605206	6	6	5	5	5	7	7	7	12	12	12	9	10	10	12
25	AK	1605549	5	5	5	5	5	9	7	7	11	11	11	9	9	10	13
26	AT	1605433	6	6	5	5	5	7	7	7	10	10	10	10	10	10	12
27	JK	1605412	6	6	5	5	5	7	6	6	12	12	12	10	10	10	12
28	SS	1602353	5	5	5	5	5	7	7	7	12	12	12	10	10	10	12
29	SK	1605312	6	6	5	5	5	8	9	8	13	13	13	10	10	9	11
30	A	1608039	6	6	5	5	5	7	7	7	13	13	13	10	9	9	12

SR. NO	NAME	MRD . NO	IMMEDIATE RECALL WEEK 3	IMMEDIATE RECALL WEEK 16	RETENTION FOR SIMILAR PAIRS WEEK 1	RETENTION FOR SIMILAR PAIRS WEEK 3	RETENTION FOR SIMLAR PAIRS WEEK 16	RETENTION FOR DISIMILAR PAIRS WEEK 1	RETENTION FOR DISIMILAR PAIRS WEEK 3	RETENTION FOR DISIMILAR PAIRS WEEK 16	VISUAL RETENTION WEEK 1	VISUAL RETENTION WEEK 3	VISUAL RETENTION WEEK 16	RECOGNITION WEEK 1	RETENTION WEEK 3	RECOGNITION WEEK 16
1	AG	1598651	12	12	4	4	4	10	10	10	12	13	12	10	10	10
2	B	1604836	12	12	5	5	4	10	10	10	13	13	13	10	9	10
3	SS	1605668	12	12	4	4	4	13	15	14	11	11	11	9	10	10
4	MK	1604881	11	12	5	5	5	10	10	10	11	11	12	9	10	10
5	MK	1604888	12	12	5	4	5	13	15	15	12	12	12	8	9	9
6	AS	1604890	10	11	4	4	4	13	13	13	13	13	13	10	10	10
7	HM	1604370	12	12	5	5	4	10	10	10	13	13	13	8	9	9
8	B	1605578	12	12	5	5	4	14	15	15	13	13	12	9	10	10
9	TS	1604517	11	12	4	4	4	10	10	10	12	12	13	10	9	10
10	CS	1604553	10	11	4	5	5	10	10	10	11	12	12	10	10	10
11	SK	1603881	12	12	4	4	4	10	10	10	10	12	12	10	10	10
12	SK	1604742	12	12	4	4	4	13	15	13	10	11	11	10	10	10
13	KV	1605516	12	12	4	4	4	10	10	10	12	12	12	10	10	10
14	JS	1605519	13	12	5	5	5	10	10	10	10	11	11	10	10	10
15	KK	1605441	13	13	5	5	5	10	10	10	12	11	11	10	10	10
16	J	1605090	12	12	4	4	5	10	10	10	12	12	12	10	9	9
17	GS	1605448	12	12	5	5	5	13	13	13	12	12	12	9	10	10
18	AS	1605574	12	12	4	4	4	10	10	10	13	13	13	10	10	10
19	RKS	1604942	12	12	4	4	4	13	14	14	12	12	12	10	10	10
20	P	1605190	12	12	4	4	4	12	12	10	12	13	13	9	10	10
21	DG	1604846	13	13	5	5	5	10	10	10	13	13	13	10	10	10
22	HS	1605241	12	13	4	4	4	10	10	10	12	12	12	10	10	10
23	SG	1605323	12	12	4	4	4	13	13	13	12	13	13	10	10	10
24	V	1605206	12	13	5	5	5	14	14	14	13	13	12	9	9	10
25	AK	1605549	13	13	5	5	5	10	10	10	13	12	12	9	9	10
26	AT	1605433	12	13	5	5	5	10	10	10	12	12	12	9	9	9
27	JK	1605412	13	13	4	4	4	10	10	10	13	13	13	10	10	10
28	SS	1602353	12	12	5	5	5	10	10	10	13	13	13	9	9	10
29	SK	1605312	11	11	5	5	5	10	10	10	12	12	12	10	10	10
30	A	1608039	12	12	5	5	5	10	10	10	13	13	13	10	10	10

SR. NO	NAME	MRD . NO	Total score of memory week1	Total score of memory week3	Total score of memory week16	Δ Total score of memory	Δ Total score of memory	DSST week1	DSST week3	DSST week16	Δ DSST week3	Δ DSST week3	NLR week 1	MLR week 1	PLR week 1	NLR Week 3	MLR Week3	PLR Week 3	NLR Week 16	MLR Week 16	PLR Week 16	Change NLR Week 3
1	AG	1598651	95	96	96	-1	-1	90	90	90	0	0	0.69	0.17	100.68	1.19	0.17	98.68	0.20	0.18	98.28	-0.50
2	B	1604836	109	103	107	6	2	83	87	88	-4	-5	1.80	0.14	136.44	2.20	0.14	134.44	1.50	0.15	134.04	-0.40
3	SS	1605668	99	103	102	-4	-3	83	83	84	0	-1	1.37	0.12	41.97	0.87	0.22	59.54	0.77	0.23	59.54	0.50
4	MK	1604881	93	97	101	-4	-8	90	90	89	0	1	1.77	0.25	146.52	1.27	0.15	144.52	1.17	0.16	144.12	0.50
5	MK	1604888	100	101	104	-1	-4	90	90	90	0	0	1.20	0.21	74.10	0.70	0.11	82.10	0.60	0.12	71.70	0.50
6	AS	1604890	109	109	106	0	3	90	90	90	0	0	1.73	0.21	68.53	1.23	0.21	76.54	1.13	0.12	66.13	0.50
7	HM	1604370	96	99	99	-3	-3	83	83	82	0	1	1.58	0.18	159.00	1.08	0.20	157.00	1.20	0.20	156.60	0.50
8	B	1605578	105	107	105	-2	0	56	58	58	-2	-2	2.17	0.14	135.18	1.67	0.14	133.18	1.57	0.15	132.78	0.50
9	TS	1604517	98	99	99	-1	-1	65	67	69	-2	-4	2.81	0.22	239.39	2.31	0.12	237.39	2.21	0.13	236.99	0.50
10	CS	1604553	96	96	98	0	-2	70	72	71	-2	-1	2.40	0.17	197.96	1.90	0.17	195.96	1.80	0.18	195.56	0.50
11	SK	1603881	101	104	106	-3	-5	86	88	88	-2	-2	0.89	0.15	77.53	1.39	0.15	85.60	1.29	0.16	87.56	-0.50
12	SK	1604742	95	100	99	-5	-4	76	77	77	-1	-1	0.55	0.21	64.96	0.05	0.18	62.96	1.95	0.19	72.56	0.50
13	KV	1605516	98	96	96	2	2	80	80	81	0	-1	2.67	0.23	71.02	2.17	0.13	69.02	2.07	0.14	68.62	0.50
14	JS	1605519	102	102	101	0	1	90	90	90	0	0	2.39	0.19	129.12	1.89	0.19	127.12	1.79	0.10	126.72	0.50
15	KK	1605441	97	97	101	0	-4	80	80	80	0	0	0.73	0.12	72.94	1.23	0.17	70.94	1.13	0.17	70.54	-0.50
16	J	1605090	101	97	99	4	2	87	87	86	0	1	2.93	0.17	86.55	2.43	0.17	84.55	2.33	0.18	84.15	0.50
17	GS	1605448	103	104	106	-1	-3	69	70	70	-1	-1	1.70	0.69	297.44	1.20	0.59	295.44	1.10	0.60	295.04	0.50
18	AS	1605574	105	106	102	-1	3	72	73	73	-1	-1	3.24	0.41	176.57	2.74	0.31	174.57	2.64	0.32	174.17	0.50
19	RKS	1604942	111	109	109	2	2	83	83	83	0	0	1.94	0.16	44.09	2.44	0.16	42.09	1.34	0.17	45.98	-0.50
20	P	1605190	101	104	102	-3	-1	84	84	84	0	0	1.51	0.13	58.88	1.01	0.18	56.88	0.91	0.14	56.48	0.50
21	DG	1604846	99	101	101	-2	-2	64	64	64	0	0	2.19	0.57	186.70	1.69	0.47	184.70	1.59	0.48	184.30	0.50
22	HS	1605241	104	104	105	0	-1	68	68	68	0	0	4.23	0.20	91.47	3.73	0.10	89.47	3.63	0.11	89.07	0.50
23	SG	1605323	103	104	104	-1	-1	89	89	90	0	-1	3.04	0.13	204.27	2.54	0.13	202.27	2.44	0.15	201.87	0.50
24	V	1605206	104	105	106	-1	-2	90	90	90	0	0	0.90	0.19	80.79	0.40	0.21	78.79	2.30	0.16	78.39	0.50
25	AK	1605549	100	97	99	3	1	78	78	78	0	0	2.37	0.25	145.06	1.87	0.15	143.06	1.77	0.16	142.66	0.50
26	AT	1605433	96	96	97	0	-1	81	81	81	0	0	1.84	0.22	217.16	1.34	0.12	215.16	1.24	0.13	214.76	0.50
27	JK	1605412	101	101	100	0	1	69	69	69	0	0	1.25	0.17	94.76	1.75	0.27	98.76	1.65	0.08	92.36	-0.50
28	SS	1602353	100	100	101	0	-1	70	70	70	0	0	3.03	0.15	144.30	3.53	0.17	142.30	2.43	0.17	141.90	-0.50
29	SK	1605312	103	104	102	-1	1	88	88	88	0	0	2.07	0.15	98.00	2.57	0.15	96.00	1.47	0.17	100.56	-0.50
30	A	1608039	104	103	103	1	1	84	84	84	0	0	1.51	0.22	142.49	1.01	0.20	145.42	0.91	0.13	140.09	0.50

SR. NO	NAME	MRD . NO	Change MLR Week 3	Change PLR Week 3	Change NLR week 16	Change MLR week 16	Change PLR week 16	ABSOLUTE NEUTROPHIL COUNT WEEK 1	ABSOLUTE LYMPHOCYTE COUNT WEEK 1	ABSOLUTE MONOCYTE COUNT WEEK	PLATELET COUNT WEEK 1	WBC WEEK 1	ABSOLUTE NEUTROPHIL COUNT Week 3	ABSOLUTE LYMPHOCYTE COUNT Week 3	ABSOLUTE MONOCYTE COUNT Week	PLATELET COUNT Week 3	WBC Week 3	NLR Week 3
1	AG	1598651	0.00	2.00	0.49	-0.01	2.40	3.19	2.69	0.72	298.23	6.60	3.48	2.43	0.79	313.15	6.70	1.44
2	B	1604836	0.00	2.00	0.30	-0.01	2.40	7.13	1.20	0.53	295.02	8.85	7.78	1.08	0.58	309.77	9.43	7.22
3	SS	1605668	-0.10	-17.57	0.60	-0.11	-17.57	6.22	3.33	0.38	172.87	9.94	6.79	2.99	0.42	181.52	10.21	2.27
4	MK	1604881	0.10	2.00	0.60	0.09	2.40	5.36	2.36	0.81	369.37	8.54	5.85	2.12	0.90	387.83	8.87	2.76
5	MK	1604888	0.10	-8.00	0.60	0.09	2.40	4.37	2.57	0.80	216.40	7.74	4.77	2.32	0.88	227.22	7.96	2.06
6	AS	1604890	0.00	-8.01	0.60	0.09	2.40	7.51	2.32	0.72	182.38	10.55	8.19	2.09	0.79	191.50	11.07	3.92
7	HM	1604370	-0.02	2.00	0.38	-0.02	2.40	4.57	2.20	0.40	372.19	7.18	4.99	1.98	0.44	390.80	7.42	2.52
8	B	1605578	0.00	2.00	0.60	-0.01	2.40	7.14	2.68	0.64	388.91	10.46	7.79	2.41	0.71	408.36	10.91	3.23
9	TS	1604517	0.10	2.00	0.60	0.09	2.40	4.86	1.47	0.47	365.53	6.79	5.30	1.32	0.52	383.81	7.14	4.02
10	CS	1604553	0.00	2.00	0.60	-0.01	2.40	4.48	1.55	0.27	352.38	6.29	4.89	1.39	0.30	370.00	6.57	3.51
11	SK	1603881	0.00	-8.07	-0.40	-0.01	-10.03	5.00	3.59	0.89	313.81	9.47	5.45	3.23	0.98	329.50	9.66	1.69
12	SK	1604742	0.03	2.00	-1.40	0.02	-7.60	4.02	3.84	0.30	287.71	8.16	4.39	3.45	0.33	302.10	8.18	1.27
13	KV	1605516	0.10	2.00	0.60	0.09	2.40	6.72	2.12	0.91	171.75	9.76	7.33	1.91	1.00	180.33	10.25	3.84
14	JS	1605519	0.00	2.00	0.60	0.09	2.40	5.24	1.81	0.53	252.11	7.59	5.72	1.63	0.59	264.72	7.94	3.51
15	KK	1605441	-0.05	2.00	-0.40	-0.05	2.40	3.60	2.93	0.34	243.17	6.88	3.93	2.64	0.37	255.33	6.94	1.49
16	J	1605090	0.00	2.00	0.60	-0.01	2.40	7.64	2.23	0.61	214.94	10.48	8.34	2.00	0.67	225.69	11.01	4.16
17	GS	1605448	0.10	2.00	0.60	0.09	2.40	4.52	1.08	0.85	330.86	6.45	4.93	0.97	0.94	347.40	6.84	5.09
18	AS	1605574	0.10	2.00	0.60	0.09	2.40	5.49	1.47	0.75	273.97	7.71	5.99	1.32	0.82	287.67	8.13	4.53
19	RKS	1604942	0.00	2.00	0.60	-0.01	-1.89	7.68	3.15	0.80	170.26	11.64	8.38	2.83	0.89	178.77	12.10	2.96
20	P	1605190	-0.05	2.00	0.60	-0.01	2.40	5.98	2.98	0.69	205.05	9.65	6.52	2.68	0.76	215.30	9.96	2.43
21	DG	1604846	0.10	2.00	0.60	0.09	2.40	2.91	1.08	0.72	320.81	4.71	3.17	0.97	0.79	336.86	4.94	3.26
22	HS	1605241	0.10	2.00	0.60	0.09	2.40	7.89	1.67	0.84	169.03	10.39	8.60	1.50	0.92	177.48	11.02	5.74
23	SG	1605323	0.00	2.00	0.60	-0.02	2.40	6.00	1.69	0.39	362.80	8.08	6.54	1.52	0.43	380.94	8.49	4.29
24	V	1605206	-0.02	2.00	-1.40	0.03	2.40	4.23	3.02	0.57	273.79	7.81	4.61	2.71	0.62	287.48	7.95	1.70
25	AK	1605549	0.10	2.00	0.60	0.09	2.40	3.04	1.06	0.37	270.15	4.47	3.32	0.95	0.40	283.65	4.67	3.48
26	AT	1605433	0.10	2.00	0.60	0.09	2.40	7.00	1.31	0.94	298.10	9.26	7.64	1.18	1.03	313.01	9.86	6.47
27	JK	1605412	-0.10	-4.00	-0.40	0.09	2.40	5.95	3.40	0.91	356.17	10.26	6.49	3.06	1.00	373.98	10.55	2.12
28	SS	1602353	-0.02	2.00	0.60	-0.02	2.40	5.43	1.54	0.23	236.95	7.19	5.92	1.38	0.25	248.80	7.56	4.28
29	SK	1605312	0.00	2.00	0.60	-0.02	-2.56	7.61	2.96	0.73	319.50	11.30	8.30	2.66	0.80	335.48	11.76	3.12
30	A	1608039	0.02	-2.93	0.60	0.09	2.40	6.97	1.71	0.89	291.43	9.58	7.60	1.54	0.98	306.00	10.13	4.93

SR. NO	NAME	MRD . NO	MLR Week 3	PLR Week 3	ABSOLUTE NEUTROPHIL COUNT WEEK 16	ABSOLUTE LYMPHOCYTE COUNT WEEK 16	ABSOLUTE MONOCYTE COUNT WEEK 16	PLATELET COUNT WEEK 16	WBC WEEK 16
1	AG	1598651	0.27	129.13	3.77	2.16	0.86	328.06	6.79
2	B	1604836	0.44	287.52	8.42	0.96	0.63	324.52	10.01
3	SS	1605668	0.12	60.63	7.36	2.66	0.46	190.16	10.48
4	MK	1604881	0.35	182.61	6.34	1.89	0.98	406.30	9.21
5	MK	1604888	0.31	98.12	5.17	2.06	0.96	238.04	8.18
6	AS	1604890	0.31	91.62	8.87	1.86	0.87	200.62	11.60
7	HM	1604370	0.18	197.17	5.41	1.76	0.48	409.41	7.65
8	B	1605578	0.24	169.37	8.44	2.14	0.77	427.80	11.35
9	TS	1604517	0.32	290.95	5.74	1.17	0.56	402.09	7.48
10	CS	1604553	0.17	265.95	5.30	1.24	0.32	387.62	6.85
11	SK	1603881	0.25	102.11	5.91	2.87	1.07	345.19	9.84
12	SK	1604742	0.08	87.45	4.75	3.07	0.36	316.49	8.19
13	KV	1605516	0.43	94.52	7.95	1.70	1.10	188.92	10.74
14	JS	1605519	0.29	162.30	6.19	1.45	0.64	277.32	8.29
15	KK	1605441	0.12	96.76	4.26	2.35	0.41	267.49	7.01
16	J	1605090	0.27	112.64	9.03	1.78	0.73	236.43	11.54
17	GS	1605448	0.79	358.68	5.34	0.86	1.03	363.94	7.23
18	AS	1605574	0.51	217.66	6.49	1.17	0.90	301.37	8.56
19	RKS	1604942	0.26	63.10	9.08	2.52	0.97	187.29	12.57
20	P	1605190	0.23	80.36	7.06	2.38	0.83	225.55	10.28
21	DG	1604846	0.67	346.15	3.44	0.87	0.86	352.90	5.16
22	HS	1605241	0.50	118.38	9.32	1.33	1.00	185.94	11.66
23	SG	1605323	0.23	249.98	7.09	1.35	0.46	399.08	8.91
24	V	1605206	0.19	105.92	4.99	2.41	0.68	301.17	8.09
25	AK	1605549	0.35	297.57	3.60	0.85	0.44	297.16	4.88
26	AT	1605433	0.72	265.01	8.28	1.05	1.13	327.91	10.46
27	JK	1605412	0.27	122.22	7.03	2.72	1.09	391.79	10.84
28	SS	1602353	0.15	180.02	6.41	1.23	0.28	260.65	7.92
29	SK	1605312	0.25	126.01	8.99	2.37	0.88	351.45	12.23
30	A	1608039	0.52	198.31	8.24	1.37	1.07	320.58	10.68

Baba Farid University
of Health Sciences
Sadiq Road
Faridkot-151 203 (Pb). INDIA.
Phone : 01639-256232,256236
Tele/Fax : 01639-256235
Email – Thesisbfuhs@gmail.com

(54)

No. BFUHS/2K23p-TH/ 39 Date 1/1/24

The Principal
Dayanand Medical College & Hospital
Ludhiana

Subject:: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 25.09.2023 has approved the plan of thesis of **Sandeep Kaur Dhillon**, a student of your college for **MD Psychiatry** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Cognitive functioning and neutrophil lymphocyte ratio (nlr), platelet lymphocyte ratio (plr) and monocyte lymphocyte ratio (mlr) in bipolar affective disorder .

Supervisor	Co-Supervisor:-	Co-Supervisor:-
Dr. Navkiran S. Mahajan	Dr. Ranjive Mahajan	Dr. Bhavna Malhotra
Professor	Prof. & Head	Professor
Dept. of Psychiatry	Dept. of Psychiatry	Dept. of Pathology

The student may submit the thesis in triplicate alongwith the plan in triplicate also, to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She may be directed to attach a photocopy of this letter with the forwarding letter while submitting thesis in the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic, if any.

Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

COGNITIVE FUNCTIONING AND NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR) AND MONOCYTE LYMPHOCYTE RATIO (MLR) IN BIPOLAR AFFECTIVE DISORDER

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

PSYCHIATRY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

AUGUST, 2022

DR. SANDEEP KAUR DHILLON

DEPARTMENT OF PSYCHIATRY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	COGNITIVE FUNCTIONING AND NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR) AND MONOCYTE LYMPHOCYTE RATIO (MLR) IN BIPOLAR AFFECTIVE DISORDER
For the degree of	M.D PSYCHIATRY
Name of the candidate	Dr. Sandeep Kaur Dhillon
Supervisor	Dr. Navkiran S. Mahajan, Professor, Department of Psychiatry, DMCH, Ludhiana
Co-supervisor(s)	Dr. Ranjive Mahajan, Professor, Department of Psychiatry, DMCH, Ludhiana. Dr. Bhavna Malhotra, Professor, Department of Pathology, DMCH, Ludhiana
Institution	Dayanand Medical College and Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Bipolar affective disorder (bipolar) is a multicomponent illness involving episodes of severe mood disturbance, neuropsychological deficits, immunological and physiological changes, and disturbances in functioning. It is one of the leading causes of disability worldwide.

Available evidence underscores that cognitive dysfunction is a critical mediator. of adverse psychosocial outcomes in BD and a predictor of unfavorable employment outcomes In this case-control study, we are studying cognitive functions in patients of bipolar disorder and Neutrophil – lymphocyte ratio (NLR), platelet – lymphocyte ratio (PLR), and monocyte lymphocyte ratio (MLR) have recently been used as markers of inflammation. Higher NLR, MLR, and PLR values have been determined during the manic episode of bipolar disorder compared to a control group.

AIM OF STUDY – to study the cognitive functioning and NLR, MLR and PLR in bipolar affective disorder.

MATERIALS AND METHODS – The study will be conducted on 100 consecutive patients in age group 18-65 years diagnosed as bipolar disorder presenting to Department of Psychiatry, DMC&H Ludhiana and 30 healthy controls in the age group of 18-65 years. Patients will be assessed in two clinical settings:

1. Neuropsychological assessment: Their cognitive functions will be assessed using neuropsychological assessment tests.
2. Hematological assessment: Their NLR, PLR AND MLR will be assessed using complete blood cell count

CLINICAL SIGNIFICANCE – the study will help us in understanding the relationship between bipolar affective disorder, cognitive functioning and NLR, PLR AND MLR. In this study, cognitive functioning and NLR, MLR, PLR of patients of bipolar disorder will be assessed and compared with healthy controls. The present study will suggest that Cognitive functioning and hematological biomarkers may play an important role in the course and prognosis of bipolar patients

Keywords: Bipolar affective disorder, cognitive functioning, neutrophil lymphocyte ratio, platelet lymphocyte ratio, monocyte lymphocyte ratio, mood stabilizer.

(Signature) Candidate | (Signature) Co-supervisor | (Signature) Co-supervisor | (Signature) Supervisor | (Signature) Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"COGNITIVE FUNCTIONING AND NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR) AND MONOCYTE LYMPHOCYTE RATIO (MLR) IN BIPOLAR AFFECTIVE DISORDER"** exist in the Department of Psychiatry, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

Supervisor

Dr. Navkiran S Mahajan
Professor
Department of Psychiatry
DMCH, Ludhiana

Co-Supervisor's

Dr. Ranjive Mahajan
Professor & Head
Department of Psychiatry
DMCH, Ludhiana

Dr. Bhavna Malhotra
Professor
Department of Pathology
DMCH, Ludhiana

Head of the Department

Dr. Ranjive Mahajan
Professor & Head
Department of Psychiatry
DMCH, Ludhiana

Place : _____
Date : _____

APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Sandeep Kaur Dhillon
Department	Psychiatry
Topic of Thesis	COGNITIVE FUNCTIONING AND NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR) AND MONOCYTE LYMPHOCYTE RATIO (MLR) IN BIPOLAR AFFECTIVE DISORDER
Likely date of appearing in PG examination	May/ June 2024
Date of enrollment	4th March, 2022
Name of Head of Department	Dr. Ranjive Mahajan
1) Supervisor **2) Co-Supervisor(s)**	Dr. Navkiran S Mahajan Dr. Ranjive Mahajan Dr. Bhavna Malhotra
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)	Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal & Professor & Head, Cardiology)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / ~~No~~

Dr. Sandeep Puri
Chairperson
Research Committee

Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee

Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	DR. SANDEEP KAUR DHILLON H.NO. 1503, NEW SODHI NAGAR, ZIRA ROAD, MOGA, 142001, PUNJAB
2	NAME OF THE INSTITUTE	DAYANAND MEDICAL COLLEGE AND HOSPITAL, LUDHIANA [PUNJAB]
3	COURSE OF STUDY AND SUBJECT	M.D PSYCHIATRY
4	DATE OF ADMISSION OF COURSE	7, MARCH,2022
5	TITLE OF THE TOPIC	"COGNITIVE FUNCTIONING AND NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR) AND MONOCYTE LYMPHOCYTE RATIO (MLR) IN BIPOLAR AFFECTIVE DISORDER."

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Bipolar disorder (BD) is a chronic psychiatric disorder characterized by the alternation of different phases, specifically hypomanic/manic and major depressive episodes and it affects 2–3% of the general population worldwide and its onset typically occurs during adolescence or early adulthood.[1] The Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) includes three main types of BD in the category of “Bipolar and related disorders”: BD type I, BD type II, and cyclothymic disorder.[1] Patients with BD type I have experienced at least one manic episode (defined as an abnormally elevated mood or irritability and related symptoms with severe functional impairment or psychotic symptoms for seven days or more), with or without major depressive episodes. Patients with BD type II have experienced at least one hypomanic episode (defined as abnormally elevated mood or irritability and related symptoms with decreased or increased function for four days) and one major depressive episode.[1] In the general population, the lifetime prevalence of BD is around 1% for BD I.[2,3] A large cross-sectional survey of 11 countries noted that the overall lifetime prevalence of bipolar spectrum disorders was 2-3%, with a prevalence of 0.4% for BD II.[4] Because of the ambiguity of its phenomenology, epidemiologic data on cyclothymia is equivocal, suggestive of a range of 0.5 to 6.3%. The mean age of onset for bipolar appears to be in the early twenties, although findings vary between 20–30 years. The contribution of genetic factors to bipolar has long been identified, with evidence from twin studies suggesting monozygotic concordance of between 40–70%, and lifetime risk in first-degree relatives is 5–10%; around seven times higher than the general population risk.[5] The inflammatory system plays an important role in the onset and progression of mood disorders, studies have evaluated NLR, MLR and PLR as potential biomarkers of different mood episodes of BD. It was found that PLR, NLR, and MLR were significantly higher in patients who were experiencing a manic episode than depressed individuals. Moreover, they are consistent with previous studies in which manic patients had higher levels of pro- inflammatory cytokines, such as C-reactive protein (CRP), soluble interleukin (IL)-6 receptor, and soluble tumour necrosis alpha (INF-o) receptor, compared to patients with major depressive episodes, suggesting more severe inflammatory dysregulation in mania. As inflammatory ratios represent economical and accessible markers of inflammation, further studies should be

conducted to consider their role as peripheral biomarkers of BD mood episodes. The cognitive deterioration is often considered as a basic characteristic of this psychiatric disorder.[6] Deficits in cognitive function are both transitory (acute phase of illness) and persistent (chronic/residual symptoms).[7] Areas such as sustained attention, memory and executive function are involved. These deficits are present during the acute phase of illness and persist through-out periods of euthymia. The mood changes in acute episodes have a clear impact on cognitive functioning. Cognitive functioning may contribute to functional outcome in bipolar disorder and may be applied in research and clinical interventions to prevent cognitive and functional impairment.[8]

Both lithium and valproate are well-established treatments for bipolar disorder. The mechanism of action of lithium is not known. It is rapidly absorbed, has a small volume of distribution, and is excreted in the urine unchanged (there is no metabolism of lithium). Lithium modifies sodium transport in nerve and muscle cells. It alters the metabolism of neurotransmitters, specifically catecholamines and serotonin.[9] It may alter intracellular signaling via second messenger systems by inhibition of inositol monophosphate. This inhibition then affects neurotransmission through the phosphatidylinositol secondary messenger system. Lithium also decreases protein kinase C activity, which alters genomic expression associated with neurotransmission. Lithium appears to increase cytoprotective proteins and possibly activates neurogenesis and increases gray matter volume. The half-life of lithium is 18 to 30 hours. Lithium can modulate granulopoiesis in concentrations 0.3-5.0 mEq/L. via pluripotent stem cell stimulation and/or enhanced production of colony-stimulating factor. Possible mechanism of lithium induced leucocytosis is elevation of plasma cortisol or/ stimulation of leucocyte precursors. Yet subtle, negative effects on psychomotor speed. Many patients administered lithium carbonate complained of mental slowness, impairment of psychomotor speed, verbal memory, executive functioning.[9]

6.2 REVIEW OF LITERATURE:

Bipolar disorder is a severe and enduring psychiatric condition which in many cases starts during early adulthood and follows a relapsing and remitting course throughout life. In many patients the disease follows a progressive path with brief periods of inter-episode recovery, sub-threshold symptoms, treatment resistance and increasing functional impairment in the biopsychosocial domains.[10]

A Study conducted in Italy recruited 294 patients affected by BD, of which 143 were experiencing hypo (manic) episode and 151 in depressive phase. A blood sample was drawn to perform CBC. Mean values of neutrophils, platelets, mean platelet volume, NLR, PLR, and MLR were significantly higher in hypo (manic) than depressed individuals. Çakir et al. reported that NLR was significantly more elevated in patients with BD than healthy controls.[11] Other studies were specifically focused on specific mood episodes, showing increased NLR and PLR values [12], as well as decreased MLR values [13] in manic patients than healthy subjects. Kalelioglu et al. instead showed increased NLR and PLR levels in BD patients than controls, but no differences between euthymic and manic phases.[14] Interestingly, elevated NLR in bipolar patients has also been associated with a reduction in cognitive functions, particularly attention.[15]

The most recent meta-analysis by Bora and colleagues 4 included 45 studies (1446 patients and 1524 healthy controls) and compared patients with bipolar disorder with healthy controls on a number of measures of neurocognition. Groups were matched for age, sex, education, and premorbid intellectual capacity. Patients with bipolar disorder performed significantly worse on 17 of 18 tests of cognitive measure in the meta-analysis: results showed medium to large effect sizes for most tests of sustained attention, psychomotor speed, verbal memory, and executive functioning. Small effect sizes were noted for continuous performance test (CPT) commission errors, digit span forward, tests of visual memory recall, and verbal recognition.[16]

Regarding cognitive functions, the studies done by Anaya et al. showed clear positive association between CR and each of the assessed domains. Hence, a bipolar patient with a higher CR maintains better capacities of attention, processing speed and working memory, concentration, verbal and visuospatial memory and executive functions, independently of the possible effects of age and chronicity. These results would be in line with the hypothesis that a higher CR implies a more efficient utilization of brain networks. Our results also indicate a positive relationship

between Cran psychosocial functioning, patients with a higher CR showing a better psychosocial functioning. Cognitive functions have been found to modulate psychosocial functioning, with the latest research highlighting that verbal memory seems to be the main cognitive capacity influencing the functioning of patients with BD.[17]

In studies conducted by Dittmann et al; The multivariate analysis of covariance (MANCOVA) indicated overall differences in neuropsychological performance between the three groups. Patients with bipolar I disorder showed significantly lower scores in psychomotor speed, working memory, verbal learning, delayed memory, and executive functions than healthy controls. Patients with bipolar II disorder showed significant deficits in psychomotor speed, working memory, visual ／ constructional abilities, and executive functions compared to controls, but not on verbal learning and delayed memory. The two patient groups did not differ significantly from each other on any domain tested.[18]

The meta-analysis of neuropsychological performance in euthymic bipolar disorder conducted by Mann-Wrobel et al. revealed considerable impairments in these individuals compared to control subjects. Their findings, however, do not support a conclusion that domains of verbal memory and executive functioning are differentially impaired in this population, as some have proposed. Rather, generally comparable impairment was observed across domains in current data, with the exception of more crystallized verbal abilities. Similarly, though less severely than in schizophrenia, it appears there is a broadly generalized cognitive impairment in euthymic bipolar disorder, with verbal ability as a possible area of preserved performance.[19]

There are three main findings in the study conducted by Pålsson et al. First, the study confirmed previous findings that clinically stable patients with bipolar disorder showed impairment in inhibition, in set-shifting, in verbal fluency and in visual recall compared to healthy age-matched controls. Bipolar patients also gave more rapid responses during the Tower test and showed impulsivity on the Color-word test, yet were slower in drawing the Rey figure. Second, there were no major differences between the type I and type II subtypes of bipolar disorder. Third, treatment with antipsychotic drugs was associated with worse performance in verbal fluency, in inhibition, in set-shifting and a longer time to draw the Rey figure.[20]

A study conducted by Mehmet akif ozdemir et al on 29 patients found an increase in both wbc counts and cortisol levels from day 3 on lithium administration compared to prelithium (baseline values).[21]

In a comparitive study conducted by Ana sabater et al. three groups of BD patients were established according to their treatment: (i) lithium monotherapy (n=29); (ii) lithium together with one or more anticonvulsants (n=28); and (iii) one or more anticonvulsants (n=16). A group of healthy controls served as the control (n=25). Neuropsychological tests were applied Results: Relative to healthy controls, BD patients showed the following: those on lithium monotherapy, but not other BD groups, had preserved short-term auditory memory, long-term memory, and attention; those who took only anticonvulsants showed worse findings in short-term visual memory, working memory, and several executive functions; and all BD patients showed worse performance in processing speed, resistance to interference, and emotion recognition.[22]

Thirty-three bipolar disorder patients (all of whom were diagnosed according to DSM-IV-TR criteria and were treated during 2003 at the Lithium Clinic Program at Santa Maria Hospital, Lleida, Spain) and 33 healthy, matched controls were cognitively assessed twice over a 2-year follow-up period. All patients were receiving the same mood-stabilizer pharmacotherapy (lithium) at the first evaluation, and they were euthymic (Hamilton Rating Scale for Depression score lower than 8 and Young Mania Rating Scale score lower than 6) for at least 3 months before both evaluations. Cognitive assessment was performed by means of a neuropsychological test battery tapping into the main cognitive domains (executive function, attention, processing speed, verbal memory, and visual memory). Repeated-measures multivariate analysis of covariance showed that there were main effects of group in the executive domain and in processing speed. Multiple linear regression analysis showed that none of the variables predicted psychosocial functioning (as measured with the Global Assessment of Functioning scale).[23]

A few studies have addressed the possibility of persistent leukocyte elevation during long-term lithium therapy. 1 year follow up study was done by J. Carmen et al . It was that observed leukocyte counts in 10 manic-depressive patients over a 1-year period after establishing prelithium leukocyte baselines. During the first few weeks, all patients showed significant increases, which persisted throughout the course of treatment. However, there was no significant correlation between plasma lithium

levels and leucocytosis. Additionally, there was a significant correlation between lithium dose and leucocytosis. Although leucocytosis is not always a consistent finding in patients on long-term lithium therapy, the persistence of white blood cell elevation in our patient population suggests that lithium might be useful in the long-term management of certain leukopenia conditions using lower-than-conventional doses.[24]

6.3 AIMS AND OBJECTIVE

- To study the cognitive functioning and NLR, MLR and PLR in bipolar affective disorder.

7.0 MATERIALS AND METHODS:

7. SOURCE OF DATA: Study will be conducted on patients diagnosed as bipolar affective disorder presenting to DMC &H Ludhiana.

7.2 METHOD OF COLLECTION OF DATA

SAMPLE COLLECTION- The study would include 100 patients in age group of 18-65 years presenting with Bipolar Affective Disorder to the Department Of Psychiatry in DMC&H Hospital, Ludhiana and 30 healthy controls in the age group of 18-65 years.

INCLUSION CRITERIA:

1. The patients with a diagnosis of bipolar affective disorder according to DSM-5 criteria presenting to DMC&H, Ludhiana.
2. Age group between 18 years to 65 years.
3. Patients who have given consent for the study.

FOR CONTROLS:

1. The patients not having any history of bipolar disorder or any other psychiatric illness.
2. Age group between 18 years to 65 years.
3. Individuals who have given consent for the study

EXCLUSION CRITERIA:

1. Any other major psychiatric disorder in patients except for bipolar affective disorder
2. History of any known uncontrolled medical comorbidity.
3. Patient receiving any anti –inflammatory treatment (non-steroidal anti-inflammatory drug, corticosteroid or other anti- inflammatory drug)
4. Female patients currently having pregnancy and lactation.
5. Patients with intake of antibiotics 2 weeks before the study or during study.
6. Patients who have not given consent for the study.

FOR CONTROLS:

1. Any on-going psychiatric or neurological disorder
2. Current treatment with any psychotropic drugs.
3. Past history of bipolar disorder, schizophrenia, recurrent depression or other psychiatric disorder.
4. A first-degree relative with schizophrenia or bipolar disorder

STUDY DESIGN: The study will be conducted on 100 consecutive patients in age group 18-65 years diagnosed as Bipolar Disorder presenting to Department of Psychiatry, DMC&H Ludhiana and 30 healthy controls in age group 18-65 years. . To be eligible, patients have to meet the inclusion criteria and provide written informed consent before enrolment. Their cognitive functions will be assessed using neuropsychological assessment tests. blood test will be performed to evaluate absolute neutrophils, lymphocyte, monocyte, eosinophil, basophil and platelet count and NLR, MLR and PLR will be calculated accordingly. The cognition and biochemical markers are to be assessed on day 1, 3 weeks and after 4 months

TOOLS:

1.PGI MEMORY SCALE:. PG- Memory Scale is included in the Battery of Brain Dysfunction. The PGI Memory Scale (PGIMS) provides a comprehensive and simple scale to measure verbal and nonverbal memories on the basis of neurological theory; very short term, short term, and long-term memories on the basis of experimental evidence and remote, recent, and immediate memories on the basis of clinical practice of evaluation of memory. It contains 10 subtests

1. Remote memory
2. Recent memory
3. Mental balance
4. Attention

S. Delayed recall

6. Immediate recall (sequential reproduction of sentences
7. Retention for similar pairs
8. Retention for dissimilar pairs
9. Visual retention
10. Recognition Psychometric Properties

Subtest1 - 1 score for each correct answer. (Maximum possible score - 7)

Subtest 2 - 1 score for each correct answer. (Maximum possible score - 5)

Subtest 3 - For the first 2 questions, 3 score if all correct within 15 sec., 2 score if takes more than 15 secs, and 1 score if 1 mistake or omission. o score for 2 or more mistakes.

For last question, 3 score if all correct within 30 sec., 2 score if it takes longer than 30 secs, 1 score if there is 1 mistake and o score if there are 2 or more mistakes. (Maximum possible score - 9)

Subtest 4 - For first question, 3-4 digits = 1 score, 5-6 digits = 2 score, (1 score for mistake), 7-8 digits = 3 score (2 score for 1 mistake and o score for more than 2 mistakes). (Maximum possible score =12)

2. **TRAIL MAKING TEST:** It is a timed Neuropsychological test that involves visual scanning and working memory. The TMT has two parts; the TMT-A (rote memory) and TMT-B (executive functioning). In each test the participant is asked to draw a line between 24 consecutive circles that are randomly arranged on a page. The TMT-A uses all numbers, whereas the TMT-B alternates numbers and letters, requiring the patient to switch between numbers and letters in consecutive order. The TMT is scored by how long it takes to complete the test. The time includes correction of errors prompted by the examiner, If the person cannot complete the test in 5 minutes, the test is discontinued. An average score for TMT-A is 29 seconds and a deficient score is greater than 78 seconds. For TMT-B, an average score, is 75 seconds and a deficient score is greater than 273 seconds. Norms have been established based on age and education.

3.DIGIT SYMBOL SUBSTITUTION TEST : The DSST requires response speed, sustained attention, visual spatial skills and set shifting. It is part of the Wechsler Adult Intelligence Scale, one of the most widely used measures of intelligence. The DSST requires that the participant fill in a series of symbols correctly coded within 90 seconds. In this test the higher the score the better the person's performance.

OUTCOME: In this case-control study, cognitive functions and MLR, PLR and NLR in patients with bipolar disorder will be assessed and compared with healthy controls. The present study will suggest that Cognitive functioning and markers of inflammation may play an important role in the course and prognosis of bipolar patients and it should be considered in both clinical and research setting related to bipolar disorder.

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. To determine whether the data is normally distributed, a Kolmogorov-Smirnov test will be used. Comparison of quantitative variables between the study groups will be done using Student t-test and Mann Whitney U test for independent samples for parametric and non-parametric data respectively. For comparing categorical data, Chi square ($\chi 2$) test will be performed and fisher exact test was

used when the expected frequency is less than 5. A probability value (p value)less than 0.05 will be considered statistically significant. All statistical calculations will be done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

CBC.

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Yes, Attached herewith.

8. LIST OF REFERENCES

1. Fusar-Poli L, Natale A, Amerio A, Cimpoesu P, Grimaldi Filioli P, Aguglia E, Amore M, Serafini G, Aguglia A. Neutrophil-to-Lymphocyte, Platelet-to-Lymphocyte and Monocyte-to-Lymphocyte Ratio in Bipolar Disorder. Brain Sci. 2021;11:58.

2. Bebbington P, Ramana R. The epidemiology of bipolar affective disorder. Soc Psychiatry Psychiatr Epidemiol. 1995;30:279-92.

3. Pini S, de Queiroz V, Pagnin D, Pezawas L, Angst J, Cassano GB, Wittchen HU. Prevalence and burden of bipolar disorders in European countries. Eur Neuropsychopharmacol. 2005;15:425-34.

4. Merikangas KR, Jin R, He JP, Kessler RC, Lee S, Sampson NA, et al. Prevalence and correlates of bipolar spectrum disorder in the world mental health survey initiative. Arch Gen Psychiatry. 2011;68:241-51.

5. Craddock N, Jones I. Genetics of bipolar disorder. *J Med Genet* 1999;36:585–94.

6. Torres IJ, DeFreitas VG, DeFreitas CM, Kauer-Sant'Anna M, Bond DJ, Horner WG, et al. Neurocognitive functioning in patients with bipolar I disorder recently recovered from a first manic episode. J Clin Psychiatry. 2010;71:1234-42.

7. Martinez-Aran A, Vieta E, Reinares M, Colom F, Torrent C, Sánchez-Moreno J, et al. Cognitive function across manic or hypomanic, depressed, and euthymic states in bipolar disorder. *Am J Psychiatry.* 2004;161:262–70.

8. Elshahawi HH, Essawi H, Rabie MA, Mansour M, Beshry ZA, et al. Cognitive functions among euthymic bipolar I patients after a single manic episode versus recurrent episodes. *J Affect Disord.* 2011;130:180-91.

9. Chokhawala K, Lee S, Saadabadi A. Lithium. [Updated 2022 May 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519062/

10. Perveen T, Haider S, Mumtaz W, Razi F, Tabassum S, Haleem DJ. Attenuation of stress-induced behavioral deficits by lithium administration via serotonin metabolism. Pharmacol Rep, 2013;65:336-42.

11 Muneer A. Bipolar Disorder: Role of Inflammation and the Development of Disease Biomarkers. Psychiatry Investig. 2016;13:18-33.

12. Çakır U, Can Tuman T, Yıldırım O. Increased neutrophil/lymphoctye ratio in patients with bipolar disorder: A preliminary study. *Psychiatr. Danub.* 2015;27:180-4.

13. Mayda H, Ahsen A, Bağcioğlu E, Öztürk A, Bahçeci B, Soyucok E, et al. Effect of increased neutrophil-to-lymphocyte ratio (NLR) and decreased mean platelet volume (MPV) values on inflammation in acute mania. Nöro Psikiyatri Arşivi. 2016;53:317.

14. Kalelioglu T, Akkus M, Karamustafalioglu N, Genc A, Genc ES, Cansiz A, Emul M. Neutrophil-lymphocyte and platelet-lymphocyte ratios as inflammation markers for bipolar disorder. Psychiatry Res. 2015;228:925-7.
15. Sağlam Aykut D, Civil Arslan F, Özkorumak Karagüzel E, Aral G, Karakullukçu S. The relationship between neutrophil-lymphocyte, platelet–lymphocyte ratio and cognitive functions in bipolar disorder. Nordic Journal of Psychiatry. 2018;72:119-23.
16. Kolleen H. Katherine E. Burdick, Ilise L, Richard SE. Psychiatric Times, Psychiatric Times. 2009;26:25.
17. Anaya C, Torrent C, Caballero FF, Vieta E, Bonnin CD, Ayuso-Mateos JL, Cognitive reserve in bipolar disorder: relation to cognition, psychosocial functioning and quality of life. Acta Psychiatrica Scandinavica. 2016;133:386-98.
18. Dittmann S, Hennig-Fast K, Gerber S, Seemüller F, Riedel M, Möller HJ, et al. Cognitive functioning in euthymic bipolar I and bipolar II patients. Bipolar disorders. 2008;10:877-87.
19. Mann-Wrobel MC, Carreno JT, Dickinson D. Meta-analysis of neuropsychological functioning in euthymic bipolar disorder: an update and investigation of moderator variables. Bipolar disorders. 2011;13:334-42.
20. Erik Pålsson, Clara Figueras, Anette GM Johansson, Carl-Johan Ekman, Björn Hultman, Josefin Östlind, Mikael Landén. Neurocognitive function in bipolar disorder: a comparison between bipolar I and II disorder and matched controls. BMC Psychiatry. 2013;13:165
21. Ozdemir MA, Ozdemir GD, Guren O. Classification of COVID-19 electrocardiograms by using hexaxial feature mapping and deep learning. BMC Medical Informatics and Decision Making. 2021;21:1-20.
22. Sabater A, Garcia-Blanco AC, Verdet HM, Sierra P, Ribes J, Villar I, et al. Comparative neurocognitive effects of lithium and anticonvulsants in long-term stable bipolar patients. Journal of affective disorders. 2016;190:34-40.
22. Mur M, Portella MJ, Martinez-Aran A, Pifarre J, Vieta E. Long-term stability of cognitive impairment in bipolar disorder: a 2-year follow-up study of lithium-treated euthymic bipolar patients. Journal of Clinical Psychiatry. 2008;69:712-9.
23. Carmen J, Okafor K, Ike E. The effects of lithium therapy on leukocytes: a 1-year follow-up study. Journal of the national medical association. 1993;85:301.

PROFORMA

S. No.

DATE-

NAME AGE GENDER

MRD NO.

MARITAL STATUS

EDUCATION OCCUPATION/ LOSS OF FUNCTION
INCOME

TYPE OF FAMILY- JOINT/NUCLEAR/LIVING ALONE

ADDRESS

CONTACT NO.

AGE OF ONSET OF BIPOLAR AFFECTIVE DISORDER

DURATION OF ILLNESS /COURSE OF ILLNESS

TIME BETWEEN ONSET OF SYMPTOMS AND SEEKING FIRST MEDICAL ADVICE

INSIGHT GRADE

NUMBER OF MOOD STABALISERS - MONOTHERAPY/POLYTHERAPY

COMPLIANCE

FAMILY HISTORY OF BIPOLAR AFFECTIVE DISORDER

FAMILY HISTORY OF ANY MENTAL ILLNESS EXCEPT BIPOLAR AFFECTIVE DISORDER

3. DIGIT SYMBOL SUBSTITUTION TEST

TRAIL MAKING TEST

PGI MEMORY SCALE

Signature of Candidate **Signature of Supervisor**

HAEMATOLOGICAL INDICES

PARAMETER	**NORMAL VALUE**
1. ABSOLUTE NEUTROPHIL COUNT:	2 – 7 $X10^3$/ ul
2. ABSOLUTE LYMPHOCYTE COUNT:	0.8 – 4 $X10^3$/ ul
3. ABSOLUTE MONOCYTE COUNT:	0.12 – 1.2 $X10^3$/ ul
4. PLATELET COUNT:	150-400 X 10^3/ ul

The reference ratio value will be calculated normal study group.

INFORMED PATIENT CONSENT

Date: _____

I……..D/o, W/o, S/o……. am willing to participate in the study **"COGNITIVE FUNCTIONING AND NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR) AND MONOCYTE LYMPHOCYTE RATIO (MLR) IN BIPOLAR AFFECTIVE DISORDER"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

……. ……

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य **"COGNITIVE FUNCTIONING AND NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR) AND MONOCYTE LYMPHOCYTE RATIO (MLR) IN BIPOLAR AFFECTIVE DISORDER"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

“COGNITIVE FUNCTIONING AND NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR) AND MONOCYTE LYMPHOCYTE RATIO (MLR) IN BIPOLAR AFFECTIVE DISORDER” ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ